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(54) Title: POLYPEPTIDES DERIVED FROM RETINOIC ACID-RELATED ORPHAN RECEPTOR (ROR), AND THEIR APPLICATIONS

(57) Abstract: The invention relates to polypeptides derived from the retinoic acid-related orphan receptor (ROR) in mammals, characterized in that they are delimited in their N-terminal extremity by an amino-acid located between positions 1 to 209, and in their C-terminal extremity by an amino-acid located between positions 450 to 452 of the rat RORB,  $\alpha$ , or  $\gamma$ , or by an amino-acid located at corresponding positions in nuclear receptor ROR of other subtypes than  $\alpha$ ,  $\beta$  and  $\gamma$ , and/or of the other mammals. The invention also relates to the use of these polypeptides, or of the molecular complexes or the crystals containing them, for carrying out: -a process for the screening of a ROR-LBD ligand which is an agonist, or an antagonist of said receptor, - or a process for the analysis of the tridimensional structure of the complexes formed with said polypeptides, molecular complexes or crystals and a particular compound.

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# POLYPEPTIDES DERIVED FROM RETINOIC ACID-RELATED ORPHAN RECEPTOR (ROR), AND THEIR, APPLICATIONS

#### Field of Invention

An aspect of this invention is to obtain crystal structure from orphan receptors by using a heterologous expression system, which will not only produce high amount of the desired protein but may also furnish a pseudo-ligand. The presence of this fortuitous molecule is important to stabilize an active agonist conformation by adding concomitantly a co-activator peptide. These two elements avoid any other non-active alternative conformations.

This method is illustrated by crystals of brain specific retinoic acid-related orphan receptor ligand binding domain (RORβ-LBD) in complex with a co-activator peptide and a fortuitous fatty acid ligand. This invention also relates to methods of using DNA sequence or derived constructions to produce proteins in order either to find out the physiological ligand or to screen for synthetic analogues. This invention also relates to methods for designing and selecting ligands that bind to the RORB and methods of using such ligands. It refers also to the use of DNA sequences of ROR\$\beta\$ or derived sequences thereof in order to identify other proteins which interact with RORB. Obviously the object of this invention is also the usage of the structure of similar or homologous proteins or protein complexes, particularly all these claims are applied to the two isotypes RORα and γ.

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## **Background of this Invention**

The orphan retinoic acid-related orphan receptor β (RORβ), also called retinoid Z receptor β (RZRβ) (NR1F2) belongs to the nuclear receptor (NR) superfamily and is expressed in areas of the central nervous system. The ligand-dependent activity of the nuclear receptor makes them obvious targets for drug design in many therapeutic areas. However in the case of orphan receptors, the ligand is not known and even the existence of a ligand is not proven. RORB was never shown to bind retinoic acid. RORB regulates genes whose products play a role in the context of sensory input integration as well as in the context of the biological clock. A behavioral phenotype of RORB -/- mice was observed and seems to be similar to the phenotype described > 40 years ago for a spontaneous mouse mutation called vacillans (Sirlin, 1956). These mice display a ducklike gait, transient male incapability to sexually reproduce and a severely disorganised retina that suffer from post-natal degeneration.

Two other closely nuclear receptors are RORα and RORγ. RORα presents 61% identity and 74% similarity with RORB. RORa is rather ubiquitously expressed (Becker-André et al., 1993) and has been demonstrated to play important roles in cerebellum development and immune response (Matysiak-Scholze and Nehls, 1997; Koibuchi and Chin., 1998). Staggerer mice were found to carry a deletion within the RORα gene that prevents translation of the ligand-binding domain. They present a severe cerebellar ataxia related to a defect in developpement of Purkinje cells. Certain functions of the immune system are also affected (Hamilton & al., 1996).

Certain functions of the immune system are also affected (Hamilton & al., 1996).  $ROR\alpha$  is also constitutively expressed during myogenesis (Lau et al., 1999).

The expression of RORy is found mainly in skeletal muscle (Hirose et al., 1994) and

is induced in the middle stage of adipocyte differentiation (Kurebayashi S., and Hirose T. 1998).

As with the other members of the nuclear receptor family, RORβ has several functional domains including a DNA binding domain (DBD), and a 250 residue ligandbinding domain (LBD) which contains the ligand -binding site, and is responsible for switching on the ligand-binding function.

It would be advantageous to devise methods and compositions for reducing the time required to discover ligands to the RORB, synthesize such compounds and administer such compounds to organisms to modulate physiological processes regulated by the ROR $\beta$  receptor or any of its isotypes  $\alpha$  or  $\beta$ .

There have been no crystals reported so far of any orphan receptor in the agonist bound conformation. The structure of USP, the insect ortholog of RXR, has been published recently. Though RXRs bind 9c-RA, USP fail to bind this ligand and must still be considered as an orphan receptor. Juvenile hormones have been proposed to be the natural ligands of USP but matter is still controversial. Nevertheless, the USP LBD structure is in an antagonist-like conformation. We report discovered the first crystal structure of the orphan receptor ligand-binding domain (ROR $\beta$ -LBD) in the agonist bound conformation, which represents the transcriptionally active form of nuclear receptor.

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#### Summary of the Invention

The invention relates to polypeptides derived from the retinoic acid-related orphan receptor (ROR) in mammals, characterized in that they comprise at least the amino-acid sequence delimited in its N-terminal extremity by the first amino acid of the H1 helix, and in its C-terminal extremity by the last amino acid of the H12 helix.

The invention relates more particularly to polypeptides derived from the retinoic acid-related orphan receptor (ROR) in mammals, characterized in that they are delimited in their N-terminal extremity by an amino-acid located between positions 1 to 209 of the rat, human, or murine ROR $\beta$ ,  $\alpha$ , or  $\gamma$ , as represented on figure 3, or by an amino-acid located at corresponding positions in nuclear receptor ROR of other subtypes than  $\alpha$ ,  $\beta$  and  $\gamma$ , and/or of other mammals, and in their C-terminal extremity by an amino-acid located between positions 450 to 452 of the rat, human, or murine ROR $\beta$ ,  $\alpha$ , or  $\gamma$ , as represented on figure 3, or by an amino-acid located at corresponding positions in nuclear receptor ROR of other subtypes than  $\alpha$ ,  $\beta$  and  $\gamma$ , and/or of other mammals.

The invention relates more particularly to polypeptides derived from the retinoic acid-related orphan receptor (ROR) in mammals, characterized in that they are delimited in their N-terminal extremity by an amino-acid located between positions 1 to 209 of the human or rat nuclear receptor ROR $\beta$ , as represented on figure 3, or by an amino-acid located at corresponding positions in nuclear receptor ROR of other subtypes, such as ROR $\alpha$ , and ROR $\gamma$ , as represented on figure 3, and/or of other mammals, and in their C-terminal extremity by an amino-acid located between positions 450 to 452 of the human or rat nuclear receptor ROR $\beta$ , as represented on figure 3, or by an amino-acid located at corresponding positions in nuclear receptor ROR of other subtypes, such as ROR $\alpha$ , and ROR $\gamma$ , and/or of other mammals.

The invention also concerns polypeptides derived from the retinoic acid-related orphan receptor (ROR) in mammals, characterized in that they are delimited in their N-terminal extremity by the methionine in position 209 of the human or rat nuclear receptor ROR $\beta$ , as represented on figure 3, or by the methionine or another amino-acid such as leucine located at a corresponding position in nuclear receptor ROR of other subtypes, such as ROR $\alpha$ , and ROR $\gamma$ , and/or of other mammals, and in its C-terminal extremity by the phenylalanine in position 450 of the human or rat nuclear receptor ROR $\beta$ , as represented on figure 3, or by the phenylalanine or another amino-acid located at a corresponding position in nuclear receptor ROR of other subtypes, such as ROR $\alpha$ , and ROR $\gamma$ , and/or of other mammals.

Advantageously, polypeptides as defined above according to the invention, are characterized in that at least the approximately 100 to 200 first amino-acids of the N-terminal part of the sequence of said receptor is deleted.

Polypeptides according to the invention defined above are more particularly characterized, in that they are polypeptides derived from the nuclear receptor ROR, wherein the binding properties of the ligand-binding domain, or LBD, of said receptor, are maintained.

The invention relates more particularly to polypeptides derived from the nuclear receptor ROR $\beta$ , of mammals, such as human or rat, these derived polypeptides comprising a polypeptide as defined above, such as the polypeptides delimited by the amino-acids located in positions 201 to 459 of the sequences of rat or human ROR $\beta$  represented on figure 3, said polypeptides being characterized in that at least one of the cysteine in position 454 or in position 458 of the amino-acid sequence of said nuclear

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receptor RORβ, as represented on figure 3, is deleted or substituted by another amino-acid, natural or not, such as alanine or serine.

The invention relates more particularly to polypeptides as defined above, characterized in that:

- the N-terminal sequence delimited by the amino-acids in position 1 to 200 of the receptor, is deleted,

- and the C-terminal sequence starting from the amino-acid in position 450 of the human or rat nuclear receptor ROR $\beta$  represented on figure 3, or from the amino-acid located at a corresponding position in nuclear receptor ROR of other subtypes, such as ROR $\alpha$ , and ROR $\gamma$ , as represented on figure 3, and/or of other mammals, and more preferably from the amino-acid in position 451, 452, or 453, is deleted.

The invention relates more particularly to polypeptides as defined above, characterized in that they correspond to the fragments of mammals ROR, and more particularly of rat, human, or murifice ROR $\beta$ ,  $\alpha$ , or  $\gamma$ , delimited in their N-terminal extremity by the amino acid located in one of the positions 201 to 209 of the ROR sequences represented on figure 3, and in their C-terminal extremity by the amino acid located in one of the positions 451 or 452, of the ROR sequences represented on figure 3.

The invention concerns more particularly polypeptides as defined above, chosen among:

- the fragment delimited by the amino acids located in positions 209 to 452 of:

. the sequence of the rat ROR $\beta$  represented on figure 3, and corresponding to SEQ ID NO : 2,

. the sequence of the human ROR $\beta$  represented on figure 3, and corresponding to SEQ ID NO : 3,

. the sequence of the human RORy represented on figure 3, and corresponding to SEQ ID NO: 4,

. the sequence of the murine ROR $\gamma$  represented on figure 3, and corresponding to SEQ ID NO : 5,

. the sequence of the human ROR $\alpha$  represented on figure 3, and corresponding to SEQ ID NO : 6,

. the sequence of the murine ROR $\alpha$  represented on figure 3, and corresponding to SEQ ID NO : 7,

- the fragment delimited by the amino acids located in positions 208 to 452 of:

35 . the sequence of the rat RORβ represented on figure 3, and corresponding to SEQ ID NO: 8,

. the sequence of the human ROR $\beta$  represented on figure 3, and corresponding to SEQ ID NO : 9,

. the sequence of the human RORγ represented on figure 3, and corresponding to SEQ ID NO: 10,

the sequence of the murine RORy represented on figure 3, and corresponding to SEQ ID NO: 11,

. the sequence of the human ROR $\alpha$  represented on figure 3, and corresponding to SEQ ID NO : 12,

. the sequence of the murine RORα represented on figure 3, and corresponding to SEQ ID NO: 13,

- the fragment delimited by the amino acids located in positions 208 to 451 of:

. the sequence of the rat ROR $\beta$  represented on figure 3, and corresponding to SEQ ID NO : 14,

50 . the sequence of the human ROR $\beta$  represented on figure 3, and corresponding to SEQ ID NO : 15,

. the sequence of the human RORγ represented on figure 3, and corresponding to SEQ ID NO: 16,

. the sequence of the murine RORγ represented on figure 3, and corresponding to SEQ ID NO: 17,

the sequence of the human ROR $\alpha$  represented on figure 3, and corresponding to SEQ ID NO : 18,

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- . the sequence of the murine ROR  $\alpha$  represented on figure 3, and corresponding to SEQ ID NO : 19,
  - the fragment delimited by the amino acids located in positions 209 to 451 of:
- the sequence of the rat ROR $\beta$  represented on figure 3, and corresponding to SEQ ID NO : 20,
  - . the sequence of the human ROR $\beta$  represented on figure 3, and corresponding to SEQ ID NO : 21,
  - . the sequence of the human RORγ represented on figure 3, and corresponding to SEQ ID NO: 22,
- 10 the sequence of the murine RORγ represented on figure 3, and corresponding to SEQ ID NO: 23,
  - . the sequence of the human ROR $\alpha$  represented on figure 3, and corresponding to SEQ ID NO : 24,
- the sequence of the murine RORα represented on figure 3, and corresponding to SEQ ID NO: 25,
  - the fragment delimited by the amino acids located in positions 201 to 451 of:
  - . the sequence of the rat ROR $\beta$  represented on figure 3, and corresponding to SEQ ID NO : 26,
  - . the sequence of the human ROR $\beta$  represented on figure 3, and corresponding to SEQ ID NO : 27,
    - . the sequence of the human ROR $\gamma$  represented on figure 3, and corresponding to SEQ ID NO : 28,
    - . the sequence of the murine ROR $\gamma$  represented on figure 3, and corresponding to SEQ ID NO : 29,
- 25 the sequence of the human RORα represented on figure 3, and corresponding to SEQ ID NO: 30,
  - . the sequence of the murine ROR $\alpha$  represented on figure 3, and corresponding to SEQ ID NO : 31,
    - the fragment delimited by the amino acids located in positions 201 to 452 of:
- 30 . the sequence of the rat ROR $\beta$  represented on figure 3, and corresponding to SEQ ID NO : 32,
  - . the sequence of the human ROR  $\beta$  represented on figure 3, and corresponding to SEQ ID NO : 33,
  - the sequence of the human ROR $\gamma$  represented on figure 3, and corresponding to SEQ ID NO : 34,
  - the sequence of the murine ROR $\gamma$  represented on figure 3, and corresponding to SEQ ID NO : 35,
  - . the sequence of the human ROR  $\alpha$  represented on figure 3, and corresponding to SEQ ID NO : 36,
- to SEQ ID NO: 37.
  - Polypeptides as defined above according to the invention, are more particularly characterized by the following characteristics:
- they have the properties of binding a ligand and of transactivation of the LBD of the receptor ROR,
  - they are soluble in aqueous solvants,
  - they are crystallisable in aqueous solvents, especially by the hanging drop vapour diffusion method, more particularly at approximately 4°C.
- or polypeptides or peptide sequences derived of those above mentioned, for example by suppression, addition or substitution of one or several amino acids, these polypeptides or peptide sequences having the characterisitics above mentioned.
  - The invention also concerns molecular complexes comprising a polypeptide as defined above, said polypeptide being in association with:
- a ROR-LBD ligand which is an agonist, such as stearic acid, or an antagonist of the ROR-LBD, such as retinoic acid,
  - and/or with a co-peptide having a sequence of approximately 15-20 amino-acids and comprising the co-activator motif LXXLL or a co-repressor motif (I/L)XX(V/I)I or

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LXX(H/I)IXXX(I/L) wherein X represents any amino acid, natural or not, such as copeptides chosen among fragments of co-activators of transcription, especially those of the p160 family, and more particularly among fragments of the co-activators SRC1, such as the fragment 686-700 of SRC1, or among fragments of co-repressors of transcription.

The invention also relates to nucleotide sequence coding for a polypeptide as defined

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The invention also relates to nucleotide sequence as defined above, associated to elements necessary for the transcription of this sequence, particularly a promoter and a terminator of transcription.

The invention also concerns vector, particularly plasmid, comprising a nucleotide

sequence as defined above.

The invention also relates to host cells, such as E.coli, transformed with a vector as

The invention also relates to a process for obtaining a polypeptide, or a molecular 15 complex, as defined above, characterized in that it comprises:

- a step of transforming host cells with a nucleotide sequence as defined above, using a vector as defined above,

- a step of cultivating the transformed host cell as defined above thus obtained, in an appropriate culture medium,

- and the recovery, and if necessary, the purification of the recombinant polypeptide

or molecular complex obtained.

The invention also relates to a crystal comprising a polypeptide according, or a

molecular complex, as defined above.

Advantageously, a crystal as defined above, is characterized in that it diffracts to at least 3 angstrom resolution and has a crystal stability within 5% of its unit cell dimensions.

Preferred crystal as defined above, is such that the ROR-LBD has the following unit cell dimensions in angstroms : a=52.302 Å, b=58.490 Å and c=106.036 Å,

 $\alpha=\beta=\chi=90$ °, and an orthorhombic space group P212121.

The invention also relates to a crystal as defined above, such as obtained by carrying out a process mentioned above, and comprising a step of crystallisation in aqueous solvents of the polypeptides, or the molecular complexes, as defined above, especially at 4°C by the hanging drop vapour diffusion method.

The invention also relates to the use of the polypeptides, or of the molecular

complexes, or of the crystals, as defined above, for carrying out:

- a process for the screening of a ROR-LBD ligand which is an agonist, or an antagonist of said receptor, or for the screening of ligands that perturb the structure of the receptor and having an effect on the recruitment of cofactors (co-activators and corepressors) and hence on gene regulation,

- or a process for the analysis of the tridimensional structure of the complexes formed with said polypeptides, molecular complexes or crystals and a particular compound.

The invention relates more particularly to the use mentioned above, for the screening of compounds acting as agonists or antagonists of ROR, said compounds being useful in the frame of the treatment of pathologies related to the central nervous system, the retinal organisation, the sensorial signal integration, the motricity, and sterility.

The invention also relates to a process for the screening of a ROR-LBD ligand which is an agonist, or an antagonist of said receptor, said process comprising the following

- contacting a polypeptide, or a molecular complex, or a crystal according, as defined above, advantageously linked to a solid support, with the particular compound susceptible to be a ROR-LBD ligand, preferably one of the said polypeptide, or molecular complex, or crystal, or tested ligand, being labelled, such as with a fluorescent, radioactive or enzymatic label,

- detection of the possible association between the said polypeptide, or molecular complex, or crystal, and the tested ligand, by measuring the used label, especially after

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rinsing the support used in the preceding step, or by mass spectrometry under non denaturing conditions.

The invention also relates to a process for the analysis of the tridimensional structure of the complexes formed with a polypeptide, or a molecular complex, or a crystal, as defined above, and a particular compound susceptible to be a ROR-LBD ligand, said process comprising the following steps:

- contacting the said polypeptide, or molecular complex, or crystal, with said

particular compound,

- crystallisation of the complex formed between the said polypeptide, or molecular complex, or crystal, and the tested ligand, especially with the vapour diffusion method, 10 and tridimensional analysis of said complex, especially with the molecular replacement
  - or tridimensional analysis of said complex in soluble state, by using an appropriate method such as NMR.
- The present invention provides crystals of an RORβ-LBD bound to a ligand and to a 15 coactivator peptide, i. e. an RORβ-LBD/ligand/peptide complex. The ligand is stearic

The crystal diffracts to 1.9 Å resolution. The crystal of RORβ-LBD preferably has at least 243 amino acid and preferably comprises amino acid sequence 208 to 451 of rat RORβ. The present invention also provides the structure coordinates of the RORβ-LBD/ligand/peptide complex. The complete coordinates are listed in Table A.

The complete coordinates of crystals of an RORβ-LBD bound to a ligand and to a coactivator peptide, i. e. an RORβ-LBD/ligand/peptide complex, wherein the ligand is

retinoic acid are listed in Table B.

The present invention also provides a method for determining at least a portion of the 25 three-dimensional structure of molecules or molecular complexes which contain at least some structurally similar features to the RORβ-LBD. It is preferred that these molecules or molecular complexes\_comprise at least a part of the ligand-binding site defined by structure coordinates of RORβ-LBD amino-acids Q228, Y229, L234, W259, Q261, C262, A263, Q265, I266, H268, A269, L299, V303, L304, R306, M307, R309, A310, 30

V318, L319, F320, E321, M329, F330, L333, L338, I339, A342, F343, V419, C420,

H423, and Y446 according to Table A or a mutant or homologue thereof.

The present invention also provides a computer comprising a computer readable form

to the coordinates contained in Table A.

The present invention further provides a binding site in RORβ-LBD for an RORβ-35 LBD agonist or antagonist ligand as well as methods for designing or selecting agonists, antagonist and/or a selective RORB receptor modulator (SRORM) of ROR using information about the crystal structures disclosed herein.

The present invention also provides a method in order to crystallize orphan receptors, which permits the determination of the ligand-binding pocket, important for the

discovery of agonists and antagonists.

## Brief description of the Drawing

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Figure 2- Nucleotide and polypeptide sequences of rat RORB LBD.

Figure 3- Sequence of the rat RORB LBD as cloned, with the secondary structural elements boxed (a helices) or drawn with an arrow (b strands). Sequences of human 50 RORβ LBD, mouse RORα LBD, human RORα LBD, mouse RORγ LBD and human RORy LBD are also given.

For comparison, the aligned sequence of human RARy LBD, which was used in order to solve the crystallographic structure is given. Residues involved in stearate binding in the case of ROR\$\beta\$ or in trans retinoic acid in the case of human RAR\beta\$ binding are in

bold. Residues within a 4 Å cut-off are surrounded by a cercle.

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Figure 4- Ribbon style drawing of the RORB LBD and the co-activator peptide. The ligand stearate is shown as a ball-and-stick figure

Figure 5- Difference (2Fo-Fc) electron density (1 $\sigma$ ).

Figure 6: Detail of the hydrogen bond network formed with the ATRA carboxylate group.

Figure 7: Superposition of stearate and ATRA in the RORβ LBD pocket.

Figure 8: binding and transactivation assays for all-trans retinoic acid

# **Detailed Description of the Invention**

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The first crystal structure of the RORβ ligand-binding domain (RORβ-LBD) has been determined to 1.9 Å resolution. Crystals of rat RORB-LBD were grown from crystallizing solutions containing 0.1 M TrisHCl pH= 8.0 and PEG 6000 15%. X-ray diffraction patterns from the crystals have the symmetry and systematic absences of the orthorhombic space group P212121 with unit cell dimensions a = 52.302 Å b = 58.490 Åand c= 106.036 Å and one molecule per asymmetric unit (Mathews Volume = 2,57 Å<sup>3</sup>Da<sup>-1</sup>). The structure was determined by the method of molecular replacement using the structure of the retinoic acid (RARy-LBD) as the search model.

The complex of RORβ-LBD with sterarate and the co-activator peptide shows the

mode of binding of the ligand to the orphan receptor in the agonist conformation. The following abbreviations are used throughout the application:

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A=Ala=Alanine

V=Val=Valine

L=Leu=Leucine

30 I=Ile=Isoleucine

P=Pro=Proline

F=Phe=Phenylalanine

W=Trp=Tryptophane

M=Met=Methionine

35 G=Gly=Glycine

S=Ser=Serine

T=Thr=Threonine

C=Cys=Cysteine

Y=Tyr=Tyrosine

40 N=Asn=Asparagine

Q=Gln=Glutamine

D=Asp=Aspartic acid

E=Glu=Glutamic acid

K=Lys=Lysine

45 R=Arg=Arginine

H=His=Histidine

"Atom type" refers to the element whose coordinates have been determined. Elements are defined by the first letter in the column.

"X, Y, Z" crystallographically define the atomic position determined for each atom.

"B" is a thermal factor that measures movement of the atom around its atomic center. "Occ" is an occupancy factor that refers to the fraction of the molecules in which each atom occupies the position specified by the coordinates. A value of "1" indicates that each atom has the same conformation, i.e., the same position, in all molecules of the crystal.

Additional definitions are set forth in the specification where necessary. 55

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The ROR $\beta$  receptor described herein is intended to include any polypeptide which has the activity of the naturally occurring ROR $\beta$ . The ROR $\beta$  and ROR $\beta$ -LBD contemplated herein includes all vertebrate and mammalian forms such as rat, mouse, pig, goat, horse, guinea pig, rabbit, monkey, orangutan and human. Such terms also include polypeptides that differ from naturally occurring forms of ROR $\beta$  and ROR $\beta$ -LBD by having amino acid deletions, substitutions, and additions, but which retain the activity of ROR $\beta$  and ROR $\beta$ -LBD, respectively. The crystal structure of the invention preferably contains at least 25%, more preferably at least 50%, more preferably at least 75%, more preferably at least 90%, more preferably at least 99%, and more preferably all of the coordinates listed in Table A. The crystal of the ROR $\beta$ -LBD/ROR $\beta$ -LBD-ligand/ROR $\beta$ -LBD-ligand-peptide of the invention preferably has the following unit cell dimensions in angstroms: a = 52.302 Å b = 58.490 Å and c = 106.036 Å and an orthorhombic space group P212121.

This includes both agonists or activators and antagonist or inhibitors of the RORB-

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The peptides referred to herein (e.g., RORβ, RORβ-LBD, and the like) may be produced by any well-known method, including synthetic method, such as solid phase, liquid phase and combination solid/liquid phase syntheses; recombinant DNA methods, including cDNA cloning, optionally combined with site directed mutagenesis; and/or purification of the natural products, optionally combined with enzymatic cleavage methods to produce fragments of naturally occurring proteins.

Advantageously, the crystallizable compositions provided by this invention are amenable to x-ray crystallography. Thus, this invention also provides the three-dimensional structure of the ROR $\beta$ -LBD/ROR $\beta$ -LBD ligand peptide complex,

particularly the complex of rat RORβ-LBD with stearic acid.

The three-dimensional structure of the RORβ-LBD/ligand complex of this invention is defined by a set of structure coordinates as set forth in Table A. The term " structure coordinates" refers to Cartesian coordinates derived from mathematical equations related to the patterns obtained on diffraction of a monochromatic beam of X-rays by the atoms (scattering centers) of a RORβ/stearate/peptide complex in crystal form. The diffraction data are used to calculate an electron density map of the repeating unit of the crystal. The electron density maps are then used to establish the positions of the individual atoms of the complex.

Those of skill in the art will understand that a set of structure coordinates for a receptor or receptor/ligand, or receptor/ligand/ peptide complex or a portion thereof, is a relative set of points that define a shape in three dimensions. Thus, it is possible that an entirely different set of coordinates could define a similar or identical shape. Moreover, slight variations in the individual coordinates will have little effect on overall shape.

The variations in coordinates discussed above may be generated because of mathematical manipulations of the structure coordinates. For example, the structure coordinates set forth in Table A could be manipulated by crystallographic permutations of the structure coordinates, fractionalization of the structure coordinates; integer additions or substractions to sets of the structure coordinates, inversion of the structure coordinates or any combination of the above.

Alternatively, modifications in the crystal structure due to mutations, additions, substitutions, and/or deletions of aminoacids, or other changes in any of the components that make up the crystal could also account for variations in structure coordinates. If such variations are within an acceptable standard error as compared to the original coordinates, the resulting three-dimensional shape is considered to be the same.

Various computational analyses are therefore necessary to determine whether a molecule or molecular complex or a portion thereof is sufficiently similar to all or parts of the RORβ receptor/stearate described above as to be considered the same. Such analyses may be carried out in current software applications, such as the Molecular Similarity application of Quanta (Molecular Simulations Inc., San Diego, CA) version

55 4.1, and as described in the accompanying User's Guide.

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The Molecular Similarity application permits comparisons between different structures, different conformations of the same structure, and different parts of the same structure. The procedure used in Molecular Similarity to compare structures is divided into four steps: 1) load the structures to be compared.; 2) define the atom equivalences in these structures; 3) perform a fitting operation; and 4) analyze the results.

Each structure is identified by a name. One structure is identified as the target (i.e., the fixed structure); all remaining structures are working structures (i.e., moving structures). Since atom equivalency within QUANTA is defined by user input, for the purpose of this invention we will define equivalent atoms as protein backbone atoms (N,  $C\alpha$ , C and O) for all conserved residues between the two structures being compared. We will also

consider only rigid fitting operations.

When a rigid fitting method is used, the working structure is translated and rotated to obtain an optimum fit with the target structure. The fitting operation uses an algorithm that computes the optimum translation and rotation to be applied to the moving structure, such that the root mean square difference of the fit over the specified pairs of equivalent atom is an absolute minimum. This number, given in angstroms, is reported by QUANTA.

For the purpose of this invention, any molecule or molecular complex that has a root mean square deviation of conserved residue backbone atoms (N, Cα, C, O) of less than 1.5 Å when superimposed on the relevant backbone atoms described by structure coordinates listed in Table A are considered identical. More preferably, the root mean square deviation is less than 1 Å. In a preferred embodiment of the present invention, the molecule or molecular complex comprises at least a portion of the ligand binding site defined by structure coordinates of RORβ-LBD amino acids Q228, Y229, L234, W259, Q261, C262, A263, Q265, I266, H268, A269, L299, V303, L304, R306, M307, R309, A310, V318, L319, F320, E321, M329, F330, L333, L338, I339, A342, F343, V419, C420, H423, and Y446 according to Table A, or a mutant or homologue of said molecule or molecular complex. For purposes of the present invention, by " at least a portion of it" it is meant all or any parts of the ligand-binding site defined by these structure coordinates. More preferred are molecules or molecular complexes comprising all or any parts of the ligand-binding site defined by structure coordinates of RORB-LBD amino acids Q228, Y229, L234, W259, Q261, C262, A263, Q265, I266, H268, A269, L299, V303, L304, R306, M307, R309, A310, V318, L319, F320, E321, M329, F330, L333, L338, I339, A342, F343, V419, C420, H423, and Y446 according to Table A, or a mutant or homologue of said molecule or molecular complex. By mutant or homologue of the molecule or molecular complex it is meant a molecule or molecular complex having a binding pocket that has a root mean square deviation from the backbone atoms of said RORβ-LBD amino acids of not more than 1.5 Angstroms.

The term "root mean square deviation" means the square root of the arithmetic mean of the squares of deviations from the mean. It is a way to express the deviation or variation from a trend or object. For purposes of this invention, the "root mean square deviation" defines the variation in the backbone of a protein or protein complex from the relevant portion of the backbone of the ROR $\beta$  portion of the complex as defined by the structure coordinates described herein. Once the structure coordinates of a protein crystal have been determined they are useful in solving the structures of other crystals or in modelling by homology other proteins particularly the two isotypes ROR $\alpha$  and  $\gamma$ .

Thus, in accordance with the present invention, the structure coordinates of a RORβ/stearate/peptide complex, and in particular a complex, and portions thereof is stored in a machine-readable storage medium. Such data may be used for a variety of purposes, such as drug discovery and x-ray crystallographic analysis or protein crystal.

Accordingly, in one embodiment of this invention is provided a machine-readable data storage medium comprising a data storage material encoded with the structure coordinates set forth in Table A.

For the first time, the present invention permits the use of structure-based or rational drug design techniques to design, select, and synthesize chemical entities, including

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inhibitory and stimulatory compounds that are capable of binding to RORB-LBD, or

any portion thereof.

One particularly useful drug design technique enabled by this invention is iterative drug design. Iterative drug design is a method for optimizing associations between a protein and a compound by determining and evaluating the three-dimensional structures of successive sets of protein/compound complexes.

Those of skill in the art will realize that association of natural ligands or substrates with the binding pockets of their corresponding receptors or enzymes in the basis of many biological mechanisms of action. The term "binding pocket" as used herein, refers to a region of a molecule or molecular complex, that, as a result of its shape, favorably associates with another chemical entity or compound. Similarly, many drugs exert their biological effects through association with the binding pockets of receptors and enzymes. Such associations may occur with all or any parts of the binding pockets. An understanding of such associations will help lead to the design of drugs having more favorable associations with their target receptor, and thus, improved biological effects. Therefore, this information is valuable in designing potential ligands or inhibitors of receptors, such as inhibitors of RORβ.

The term "associating with" refers to a condition of proximity between chemical entities or compounds, or portions thereof. The association may be non-covalent-wherein the juxtaposition is energetically favored by hydrogen bonding or van der

Waals or electrostatic interactions -- or it may be covalent.

In iterative drug design, crystals of a series of protein/compound complexes are obtained and then the three-dimensional structures of each complex is solved. Such an approach provides insight into the association between the proteins and compounds of each complex. This is accomplished by selecting compounds with inhibitory activity, obtaining crystals of this new protein/compound complex, solving the three dimensional structure of the complex, and comparing the associations between the new protein/compound complex and previously solved protein/compound complexes. By observing how changes in the compound affected the protein/compound associations, these associations may be optimized.

In some cases, iterative drug design is carried out by forming successive proteincompound complexes and then crystallizing each new complex. Alternatively, a preformed protein crystal is soaked in the presence of an inhibitor, thereby forming a protein/ compound complex and obviating the need to crystallize each individual

protein/compound complex.

As used herein, the term "soaked" refers to a process in which the crystal is transferred

to a solution containing the compound of interest.

The structure coordinates set forth in Table A can also be used to aid in obtaining structural information about another crystallized molecule or molecular complex. This may be achieved by any of a number of well-known techniques, including molecular

The structure coordinates set forth in Table A can also be used for determining at least a portion of the three-dimensional structure of molecules or molecular complexes which contain at least some structurally similar features to RORB. In particular, structural information about another crystallized molecule or molecular complex may be obtained. This may be achieved by any of a number of well-known techniques, including molecular replacement.

Therefore, in another embodiment this invention provides a method of utilizing molecular replacement to obtain structural information about a crystallized molecule or molecular complex whose structure is unknown comprising the steps of:

a) generating an X-ray diffraction pattern from said crystallized molecule or molecular

b) applying at least a portion of the structure coordinates set forth in Table A to the Xray diffraction pattern to generate a three-dimensional electron density map of the molecule or molecular complex whose structure is unknown; and

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c) using all or a portion of the structure coordinates set forth in Table A to generate homology models of RORβ-LBD or any other nuclear orphan or hormone receptor ligand-binding domain.

By using molecular replacement, all or part of the structure coordinates of the RORB-LBD/RORβ-LBD-ligand/RORβ-LBD-ligand-peptide complex provided by invention or molecular complex whose structure is unknown more quickly and

efficiently than attempting to determine such information ab initio.

Molecular replacement provides an accurate estimation of the phases for an unknown structure. Phases are factors in equations used to solve crystal structures that cannot be determined directly. Obtaining accurate values for the phases, by methods other than molecular replacement, is a time-consuming process that involves iterative cycles of approximations and refinements and greatly hinders the solution of crystal structures. However, when the crystal structure of a protein containing at least a homologous portion has been solved, the phases from the known structure provide a satisfactory estimate of the phases for the unknown structure.

Thus, this method involves generating a preliminary model of a molecule or molecular complex whose structure coordinates are unknown, by orienting and positioning the relevant portion of the RORβ-LBD/RORβ-LBD ligand complex according to Table A within the unit cell of the crystal of the unknown molecule or molecular complex so as best to account for the observed X-ray diffraction pattern of the cristal of the molecule or molecular complex whose structure is unknown. Phases can then be calculated from this model and combined with the observed X-ray diffraction pattern amplitudes to generate an electron density map of the structure whose coordinates are unknown. This, in turn, can be subjected to any well-known model building and structure refinement techniques to provide a final, accurate structure of the unknown crystallized molecule or molecular complex [E. Lattman, "Use of the Rotation and Translation Functions", in Meth. Enzymol., 115, pp55-77 (1985); M. G. Rossmann, ed., "The Molecular Replacement Method", Int. Sci. Rev. Set., No 13, Gordon & Breach, New York (1972)].

The structure of any portion of any crystallized molecule or molecular complex that is sufficiently homologous to any portion of the RORβ-LBD/RORβ-LBD ligand complex

can be solved by this method.

The structure coordinates are also particularly useful to solve the structure of crystals of RORβ-LBD/RORβ-LBD ligand or RORβ-LBD ligand peptide co-complexed with a variety of chemical entities. This approach enables the determination of the optimal sites for interaction between chemical entities, including interaction of candidate RORB inhibitors with the complex. For example, high resolution X-ray diffraction data collected from crystals exposed to different types of solvent allows the determination of where each type of solvent molecule resides. Small molecules that bind tightly to theses sites can then be designed and synthesized and tested for their RORB inhibition activity.

All of the complexes referred to above may be studied using well-known X-ray difraction techniques and may be refined versus 1.5-3 Å resolution X-ray data to an Rvalue of about 0.20 or less using computer software, such as X-PLOR [Yale University, 1992, distributed by Molecular Simulations, Inc.; see, e.g., Blundell & Johnson, supra; Meth. Enzymol., vol. 114 & 115, H. W. Wyckoff et al., eds., Academic Press (1985)]. This information may thus be used to optimize known RORB agonists/antagonists, and

more importantly, to design new RORB agonists/antagonists.

Accordingly, the present invention is also directed to a binding site in RORB-LBD agonist or antagonist ligand in which a portion of RORβ-LBD ligand is in van der Waals contact or hydrogen bonding contact with at least one of the following residues: Q228, Y229, L234, W259, Q261, C262, A263, Q265, I266, H268, A269, L299, V303, L304, R306, M307, R309, A310, V318, L319, F320, E321, M329, F330, L333, L338, 1339, A342, F343, V419, C420, H423, and Y446 of RORβ-LBD. For purposes of this invention, by RORβ-LBD binding site it is also meant to include mutants or homologues thererof. In a preferred embodiment, the mutants or homologues have at least 25% identity, more preferably 50% identity, more preferably 75% identity, and most preferably 95% identity to residues Q228, Y229, L234, W259, Q261, C262, A263, Q265, I266, H268, A269, L299, V303, L304, R306, M307, R309, A310, V318, L319,

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F320, E321, M329, F330, L333, L338, I339, A342, F343, V419, C420, H423, and

Y446 of RORβ-LBD binding sites.

The present invention is also directed to a machine readable data storage medium. comprising a data storage material encoded with machine readable data, wherein the data is defined by the structure coordinates of an RORB-LBD/RORB-LBD ligand according to Table A or a homologue of said complex, wherein said homologue comprises backbone atom that have a root mean square deviation from the backbone atoms of the complex of not more than 3.0 Å. Preferably, the machine readable data storage medium, according to the invention, is wherein said molecule or molecular complex is defined by the set of structure coordinates for RORβ-LBD/RORβ-LBD ligand according to Table A, or a homologue of said molecule or molecular complex, said homologue having a root mean square deviation from the backbone atoms of said aminoacids of not more than 2.0 Å. In a preferred embodiment the machine readable data storage medium comprises a data storage medium comprising a data storage material encoded with a first set of machine readable data comprising a Fourier transform of at least a portion of the structural coordinates for a RORβ-LBD/ RORβ-LBD ligand/ RORβ-LBD ligand peptide according to Table A; which, when combined with a second set of machine readable data comprising an X-ray diffraction pattern of a molecule or molecular complex of unknown structure, using a machine programmed with instructions for using said first set of data and said second set of data, can determine at least a portion of the structure coordinates corresponding to the second set of machine readable data, said first set of data and said second set of data.

The present invention also provides for computational methods using three dimensional models of the ROR $\beta$  receptor that are based on crystals of ROR $\beta$ -LBD/ROR $\beta$ -LBD ligand complex. Generally the computational method of designing an ROR $\beta$  ligand determines which amino acid or amino acids of the ROR $\beta$ -LBD interact with a chemical moiety (at least one) of the ligand using a three dimensional model of a crystallized protein comprising the ROR $\beta$ -LBD with a bound ligand, and selecting a chemical modification (at least one) of the chemical moiety to produce a second chemical moiety with a structure that either decreases or increases an interaction between the interacting amino acid and the second chemical moiety compared to the interaction between the interacting amino acid and the corresponding chemical moiety

on the natural hormone.

The computational methods of the present invention are for designing ROR $\beta$  synthetic ligands using such crystal and three dimensional structural information to generate synthetic ligands that modulate the conformational changes of the ROR $\beta$  LBD. These computational methods are particularly useful in designing an antagonist or partial agonist to the ROR $\beta$ , wherein the antagonist or partial agonist has an extended moiety that prevents any one of a number of ligand-induced molecular events that alter the receptor's influence on the regulation of gene expression, such as preventing the normal coordination of the activation domain observed for a naturally occurring ligand or other ligands that mimic the naturally occurring ligand, such as an agonist. As described herein, synthetic ligands of the ROR $\beta$  receptor will be useful in modulating ROR $\beta$  activity in a variety of medical conditions.

RORβ is known to comprise various domains as follows:

1) a variable amino-terminal domain;

2) a highly conserved DNA-binding domain (DBD); and

3) a less conserved carboxyl-terminal ligand-binding domain (LBD).

This modularity permits different domains of each protein to separately accomplish different functions, although the domains can influence each other. The separate function of a domain is usually preserved when a particular domain is isolated from the remainder of the protein. Using conventional protein chemistry techniques a modular domain can sometimes be separated from the parent protein. Using conventional molecular biology techniques each domain can usually be separately expressed with its original function intact or chimeraes of two different nuclear receptors can be constructed, wherein the chimerae retain the properties of the individual functional domains of the respective nuclear receptors from which the chimerae were generated.

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Amino-Terminal Domain

The amino-terminal domain is the least conserved of the three domains. This domain is involved in transcriptional activation and in some cases its uniqueness may dictate selective receptor-DNA binding and activation of target genes by specific receptors isoforms. This domain can display synergistic and antagonistic interactions with the domains of the LBD. For example, studies with mutated and/or deleted receptors show positive cooperativity of the amino and carboxy terminal domains.

In some cases, deletion of either of these domains will abolish the receptor's

transcriptional activation functions.

DNA-Binding Domain

The DBD is the most conserved domain. The DBD contains two perpendicularly oriented  $\alpha$ -helices that extend from the base of the first and second zinc fingers. The two zinc fingers function in concert along with non-zinc finger residues to direct nuclear receptors to specific target sites on DNA and to align receptor homodimer to heterodimer interfaces. Various amino acids in DBD influence spacing between two half sites for receptor dimer binding.

Ligand-binding domain

The LBD is the second most highly conserved domain. Whereas integrity of several different LBD sub-domains is important for ligand binding, truncated molecules containing only the LBD retain normal ligand-binding activity. This domain also participates in other functions, including dimerization, nuclear translocation and transcriptional activation. Importantly, this domain binds the ligand and undergoes ligand-induced conformational changes as detailed herein.

As described herein, the LBD of RORB can be expressed, crystallized, its three dimensional structure determined with a ligand bound (either using crystal data from the same receptor or a different recepter or a combination thereof), and computational methods used to design ligands to its LBD, particularly ligands that contain an

extension moiety that coordinates the activation domain of RORB.

Once a computationaly designed ligand (CDL) is synthesized, it can be tested using assays to establish its activity as an agonist, partial agonist or antagonist, and affinity, as described herein. After such testing, the CDLs can be further refined by generating LBD crystals with a CDL bound to the LBD. The structure of the CDL can then be further refined using the chemical modification methods described herein for three dimensional models to improve the activity or affinity of the CDL and make a second generation CDLs with improved properties, such as that of a super agonist or antagonist.

Typically RORβ-LBD is purified to homogeneity for crystallisation. Purity of RORβ-LBD is measured with SDS-PAGE and mass spectrometry. The purified RORB for crystallization should be at least 97.5% pure or 97.5% pure, preferably at least 99.0%

pure or 99.0% pure, more preferably at least 99.5% pure or 99.5% pure.

Initially purification of the receptor can be obtained by conventional techniques, such as affinity chromatography and gel filtration chromatography.

To achieve higher purification for improved crystals of RORβ, it will be desirable to ligand shift purify the nuclear receptor using a column that separates the receptor according to charge, such as an ion exchange or hydrophobic interaction column, and then bind the eluted receptor with a ligand, especially an agonist. The ligand induces a change in the receptor's surface charge such that when rechromatographed on the same column, the receptor then elutes at the position of the liganded receptor and is removed by the original column run with the unliganded receptor. Usually saturating concentrations of ligand are used in the column and the protein can be preincubated with the ligand prior to passing it over the column.

Some developed methods involve engineering a "tag" such as with histidine placed on the end of the protein, such as on the amino terminus, and then using a cobalt chelation column for purification, Chaga, G., Biotech. Appl. Biochem. 29: 13811-13814 (1991)

incorporated by reference.

To determine the three dimensional structure of a RORβ-LBD, it is desirable to co-55 crystallize the LBD with a corresponding LBD ligand.

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Typically purified ROR\u00e3-LBD is equilibrated at a saturating concentration of ligand at a temperature that preserves the integrity of the protein. Ligand equilibration can be established between 2 and 37°C, although the receptor tends to be more stable in the 2-20°C range.

However if the ligand is unknown it is possible to co-crystallize the RORB-LBD with a fortuitous ligand coming from the heterologous expression system i.e. Escherichia coli and by adding concomitantly a co-activator peptide.

Preferably crystals are made with the hanging drop methods. Regulated temperature control is desirable to improve crystal stability and quality. Temperatures between 4 and 25°C are generally used and it is often preferable to test crystallization over a range of temperatures. It is preferable to use crystallization temperatures from 18°C to 25°C, more preferably 20 to 23°C, and most preferably 22°C.

Ligands that interact with RORβ can act as agonists, antagonists and partial agonists

based on what ligand-induced conformational changes take place. 15

Agonists induce changes in receptors that place them in an active conformation that allows them to influence transcription, either positively or negatively. There may be several different ligand induced changes in the receptor's conformation.

Antagonists, bind to receptors, but fail to induce conformational changes that leads to the receptor's transcriptionally active form or physiologically relevant conformations. Binding of an antagonist can also block the binding and therefore the actions of an agonist.

Partial agonists bind to receptors and induce only part of the changes in the receptors that are induced by agonists. The differences can be qualitative or quantitative. Thus, a partial agonist may induce some of the conformation changes induced by agonists, but

not others, or it may only induce certain changes to a limited extent.

As described herein, the unliganded receptor is in a configuration that is either inactive, has some activity or has repressor activity. Binding of agonist ligands induces conformational changes in the receptor such that the receptor becomes more active, either to stimulate or repress the expression of the genes. The receptors may also have non-genomic actions, some of the known types of changes and/or the sequences of these are listed herein.

Ligand binding by the receptor is a dynamic process, which regulates receptor

35 function by inducing an altered conformation.

The three-dimensional structure of the liganded RORB receptor will greatly aid in the development of new RORB synthetic ligands. In addition, RORB is overall well suited to modern methods including three dimensional structure elucidation and combinatorial chemistry such as those disclosed in EP 335 628, U.S. patent 5, 463,564, which are incorporated herein by reference. Computer programs that use crystallographic data when practising the present invention will enable the rational design of ligand to RORB.

Programs such as RASMOL can be used with the atomic coordinates from crystals generated by practicing the invention or used to practice the invention by generating three dimensional models and/or determining the structures involved in ligand binding. Computer program such as INSIGHT and GRASP allow further manipulation and the ability to introduce new structures. In addition, high throughput binding and bioactivity assays can be devised using purified recombinant protein and modern reporter gene transcription assays described herein and known in the art in order to refine the activity of a CDL.

Generally, the computational method of designing a ROR\$\beta\$ synthetic ligand comprises 50 two steps:

1) determining which amino acid or amino acids of RORB-LBD interacts with a first chemical moiety (at least one) of the ligand using a three dimensional model of a

crystallized protein comprising an RORβ-LBD with a bound ligand; and

2) selecting a chemical modifications (at least one) of the first chemical moiety to produce a second chemical moiety with a structure to either increase or decrease an interaction between the interacting amino acid and the second chemical moiety

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compared to the interaction between the interacting amino acid and the first chemical moiety.

Preferably the method is carried out wherein said three dimensional model is generated by comparing isomorphous ligand derivatives to produce improved phasing. Also preferred is wherein said selecting uses said first chemical moiety that interacts with at least one of the interacting amino acids Q228, Y229, L234, W259, Q261, C262, A263, Q265, I266, H268, A269, L299, V303, L304, R306, M307, R309, A310, V318, L319, F320, E321, M329, F330, L333, L338, I339, A342, F343, V419, C420, H423 or Y446.

As shown herein, interacting amino acids form contacts with the ligand and the center of the atoms of the interacting amino acids are usually 2 to 4 angstroms away from the center of the atoms of the ligand. Generally these distances are determined by computer as discussed herein and in Mc Ree 1993, however distances can be determined manually once the three dimensional model is made. See also Renaud et al., Nature 378, 681-689

(1995) for stereochemical figures of three dimensional models. More commonly, the atoms of the ligand and the atoms of interacting amino acids are 3 to 4 angstroms apart. The invention can be practiced by repeating step 1 and 2 to refine the fit of the ligand to the LBD and to determine a better ligand, such as an agonist. The three dimensional model of RORβ can be represented in two dimensions to determine which amino acids contact the ligand and to select a position on the ligand for chemical modification and changing the interaction with a particular amino acid compared to that before chemical modification. The chemical modification may be made using a computer, manually using a two dimensional representation of the three dimensional model or by chemically synthesizing the ligand. The ligand can also interact with distant amino acids after chemical modification of the ligand to create a new ligand. Distant amino acids are generally not in contact with the ligand before chemical modification. A chemical modification can change the structure of the ligand to make a new ligand that interacts with a distant amino acid usually at least 4.5 angstroms away from the ligand, preferably whereinsaid first chemical moiety is 6 to 12 angstroms away from a distant amino acid. Often distant amino acids will not line the surface of the binding activity for the ligand, they are too far away from the ligand to be part of a pocket or binding cavity. The interaction between a LBD amino acid and an atom of an LBD ligand can be made by any force or attraction described in nature. Usually the interaction between the atom of the amino acid and the ligand will be the result of a hydrogen bonding interaction, charge interaction, hydrophobic interaction, van der Waals interaction or dipole interaction. In the case of the hydrophobic interaction it is recognized that is not a per se interaction between the amino acid and ligand, but rather the usual result, in part, of the repulsion of water or other hydrophilic

computationally or using thermodynamic or kinetic methods as known in the art.

Chemical modifications will often enhance or reduce interactions of an atom of a LBD amino acid and an atom of an LBD ligand. Steric hindrance will be a common means of changing the interaction of the LBD cavity with the activation domain.

group from a hydrophobic surface. Reducing or enhancing the interaction of the LBD and a ligand can be measured by calculating or testing binding energies,

The present invention also provides methods for identifying compounds that modulates RORβ activity. Various methods or combination thereof can be used to identify these compounds. For example, test compounds can be modeled that fit spatially into the RORβ-LBD as defined by structure coordinates according to Table A, or using a three-dimensional structural model of RORβ-LBD, mutant RORβ-LBD, or RORβ-LBD homolog or portion thereof. Structure coordinates of the ligand binding site, in particular amino acids Q228, Y229, L234, W259, Q261, C262, A263, Q265, I266, H268, A269, L299, V303, L304, R306, M307, R309, A310, V318, L319, F320, E321, M329, F330, L333, L338, I339, A342, F343, V419, C420, H423, or Y446 can also be used to identify structural and chemical features. Identified structural or chemical features can then be employed to design or select compounds as potential RORβ modulators. By structural and chemical features it is meant to include, but is not limited to, van der Waals interactions, hydrogen bonding interactions, charge

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interaction, hydrophobic bonding interaction, charge interaction, hydrophobic interaction and dipole interaction. Alternatively, or in conjunction, the three-dimensional structural model or the ligand binding site can be employed to design or select compounds as potential RORβ modulators. Compounds identified as potential RORβ modulators can then be synthesized and screened in an assay characterized by binding of a test compound to the RORβ-LBD. Examples of assays useful in screening of potential ROR modulators include, but are not limited to screening in silico, *in vitro* assays and high throughput assays. Finally, these methods may also involve modifying or replacing one or more amino acids from RORβ-LBD such as Q228, Y229, L234, W259, Q261, C262, A263, Q265, I266, H268, A269, L299, V303, L304, R306, M307, R309, A310, V318, L319, F320, E321, M329, F330, L333, L338, I339, A342, F343, V419, C420, H423, or Y446 of RORβ-LBD according to Table A.

A preferred method of the invention can be described as a computational method of

designing an ROR antagonist from an ROR receptor agonist comprising:

1) determining a structure of a molecular recognition domain of said agonist using a three dimensional model of a crystallized protein comprising an RORLBD, and

2) selecting at least one chemical modification of said agonist that provides a ligand structure that extends beyond a binding site for said agonist and in the direction of at least one protein domain important in RORB biological function.

Another preferred method of the invention can be described as a computational method of designing a selective  $ROR\beta$  receptor modulator such as a ROR receptor

super agonist or antagonist comprising:

1) determining at least one interacting amino acid of an RORβ-LBD that interacts with at least one first chemical moiety of said ligand using a three dimensional model of a crystallized protein comprising RORβ-LBD with a bound ligand, and

2) selecting at least one chemical modification of said first chemical moiety to produce a second chemical moiety with a structure to reduce or enhance an interaction between said interacting amino acid and said second chemical moiety compared to said

interaction between said interacting amino acid and said first chemical moiety.

However, as will be understood by those of skill in the art upon this disclosure, other structure based design methods can be used. Various computational structure based

design methods have been disclosed in the art.

For example, a number computer modeling systems are available in which the sequence of the  $ROR\beta$ -LBD and the  $ROR\beta$ -LBD structure (i.e., atomic coordinates of  $ROR\beta$ -LBD and/or the atomic coordinates of the ligand binding site, the bond and dihedral angles, and distances between atoms in the active site such as provided in Table A) can be input. This computer system then generates the structural details of the site in which a potential  $ROR\beta$  modulator binds so that complementary structural details of the potential modulators can be determined. Design in these modeling systems is generally based upon the compound being capable of physically and structurally associating with  $ROR\beta$ -LBD. In addition, the compound must be able to assume a conformation that allows it to associate with  $ROR\beta$ -LBD. Some modeling systems estimate the potential inhibitory or binding effect of a potential ROR modulator prior to actual synthesis and testing.

Methods for screening chemical entities or fragments for their ability to associate with RORβ-LBD are also well known. Often these methods begin by visual inspection of the active site on the computer screen. Selected fragments or chemical entities are then positioned with the RORβ-LBD. Docking is accomplished using software such as QUANTA and SYBYL, following by energy minimization and molecular dynamics with standard molecular mechanic forcefields such as CHARMM and AMBER. Examples of computer programs which assist in the selection of chemical fragment or chemical entities useful in the present invention include, but are not limited to, GRID (Goodford, P. J.J. Med. Chem. 1985 28: 849-857), AUTODOCK (Goodsell, D.S. and Olsen, A.J. Proteins, Structure, Functions, and Genetics 1990 8: 195-202), and DOCK (Kunts et al. J. Mol. Biol. 1982 161:269-288).

Upon selection of preferred chemical entities or fragments, their relationship to each other and ROR\u03c3-LBD can be visualized and then assembled into a single potential

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modulator. Programs useful in assembing the individual chemical entities include, but are not limited to CAVEAT (Bartlett et al. Molecular Recognition in Chemical and Biological Problems Special Publication, Royal Chem. Soc. 78, 00. 182-196 (1989) and 3D Database systems (Martin, Y.C. J. Med.Chem. 1992 35:2145-2154).

Alternatively, compounds may be designed de novo using either an empty active site or optionaly including some portion of a known inhibitor. Methods of this type of design include, but are not limited to LUDI (Bohm H-J, J. Comp. Aid. Molec. Design 1992 6:61-78) and LeapFrog (Tripos Associates, St. Louis MO).

The present invention is also directed to a RORβ-LBD selective RORβ modulator (SRORM), in particular an agonist or antagonist, identified by a computational process of the invention.

The present invention is further directed to a method for treating a ROR related disease comprising administering an effective amount of an antagonist identified by a computational process of the invention.

The present invention is also direct to a method for treating a ROR related disease comprising administering an effective amount of an agonist identified by a computational process of the invention.

Compounds identified as agonists, antagonists or SRORMs by the methods disclosed herein which are active when given orally can be formulated as liquids for example syrups, suspensions or emulsions, tablets, capsules and lozenges. A liquid composition will generally consist of a suspension or solution of the compound in a suitable liquid carrier(s), for example ethanol, glycerin, sorbitol, non-aqueous solvent such as polyethlene glycol, oils or water, with a suspending agent, preservative, surfactant, wetting agent flyvoring or coloring agent.

wetting agent, flavoring or coloring agent. Alternatively, a liquid formulation can be prepared from a reconstitutable powder. For 25 example a powder containing active compound, suspending agent, sucrose and a sweetener can be reconstituted with water to form a suspension; a syrup can be prepared from a powder containing active ingredient, sucrose and a sweetener. A composition in the form of a tablet can be prepared from a powder containing active ingredient, sucrose and a sweetener. A composition in the form of a tablet can be prepared using any 30 suitable pharmaceutical carrier(s) routinely used for preparing solid compositions. Examples of such carriers include magnesium stearate, starch, lactose, sucrose, microcrystalline cellulose, binders, for example polyvinylpyrrolidone. The tablet can also be provided with a color film coating, or colorincluded as part of the carrier(s). In addition, active compound can be formulated in a controlled release dosage form as a 35 tablet comprising a hydrophilic or hydrophobic matrix. A composition in the form of a capsule can be prepared using routine encapsulation procedures, for example by incorporation of active compound and excipients into a hard gelatin capsule. Alternatively, a semi-solid matrix of active compound and high molecular weight polyethylene glycol can be prepared and filled into a hard gelatin capsule; or a solution 40 of active compound in polyethylene glycol or a suspension in edible oil, for example liquid paraffin or fractionated coconut oil can be prepared and filled into a soft gelatin capsule. Compounds identified by the processes described herein which are active when given parenterally can be formulated for intramuscular or intravenous administration. A 45 typical composition for intra-muscular administration will consist of a suspension or solution of active ingredient in an oil, for example arachis oil or sesame oil. A typical

solvent, for example polyethylene glycol and, optionally, a chelating agent, for example, sodium metabisulphite.

Alternatively, the solution can be freeze dried and then reconstituted with a suitable solvent just prior to administration. Identified compounds which are active on rectal administration can be formulated as suppositories. A typical suppository formulation will generally consist of active ingredient with a binding and/or lubricating agent such as a gelatin or cocoa butter or other low melting vegetable or synthetic wax or fat. Identified compounds which are active on topical administration can be formulated as

transdermal compositions. Such compositions include, for example, a backing, active

composition for intravenous administration will consist of a sterile isotonic aqueous solution containing, for example active ingredient, dextrose, sodium chloride, a co-

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compound reservoir, a control membrane, liner and contact adhesive. The typical daily dose of a varies according to individual needs, the condition to be treated and with the route of administration. Suitable doses are in the general range of 0.001 to 10mg/kg bodyweight of the recipient per day.

The following examples are to illustrate the invention, but should not be interpreted as

a limitation thereon.

#### Examples

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# Cloning, Expression and Purification of the ROR $\beta$ Ligand-Binding Domain

A cDNA for expression of the ligand-binding domain of the rat RORβ-LBD (RORβ-LBD) was constructed using the pet15b vector (Novagen) to include an N-terminal polyhistidine tag and a thrombin cleavage site. E. coli BL21 (DE3) cells were grown in LBM at 37 °C to an OD 0.6 and induced with 0.8mM IPTG. The incubation was maintained at 16 °C overnight. Cells were harvested ans stored at -20°C. A total of 6-9 mg of recombinant RORβ-LBD was isolated from a 6 gram cell pellet following sonication and chromatography on a cobalt-chelate resin. Polyhistidine-tagged RORβ-LBD of approximately 90% purity eluted in a gradient of 0 to 1M imidazole. Gel filtration was performed with a Superdex S-200 Hiload 16:60 from Pharmacia. Polyhistidine-tagged rRORβ-LBD of more than 95% purity and homogeneity as checked by SDS-PAGE was concentrated to 5.8 mg/ml in 20mM TrisHCl pH=8.5, 5mMDTT, 2 mM Chaps and 100mM NaCl.

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#### Crystallization

The ROR $\beta$ -LBD stearate complex was crystallized at 22°C by vapor diffusion in the hanging-drop mode. In the crystallisation trials, the protein was used without further purification and co-crystallized with a 3-molar excess of SRC-1686-700(RHKILHRLLQEGSPS) NR-interacting peptide co-activator sequence. Addition of the peptide was crucial to obtain crystals. In the initial trial to obtain crystallization conditions, a sparse matrix crystallization screen was done with a home screen. For each crystallization trial, a 4  $\mu$ l drop was prepared by mixing 2  $\mu$ l of purified protein (5.8 mg/ml) with an equal volume of reservoir solution. The reservoir contained 500  $\mu$ l of the precipitating solution. A crystal measuring 110 x 60 x 30 mm at 22 °C in PEG 6000 15% and 100 mM Tris HCl at pH=8.0 grew within about 2 weeks. This crystal was used in a first data collection run (as described below).

#### Data Collection and Reduction

The crystals were cryoprotected by equilibration in 15 % PEG 6000 at pH 8.0 containing 15 % glycerol and then flash frozen in liquid ethane at liquid nitrogen temperature. X-ray diffraction data were collected at liquid nitrogen temperature from a single frozen crystal at the ID14-3 beamline at the ESRF Grenoble, France. Crystals diffracted Xrays to a resolution limit of 1.9 Å. All data were integrated and scaled using DENZO and SCALEPACK (Otwinowski and Minor, 1997). The data set between 30 and 3.4 Å shows a completeness of 88.9 % resolution with an Rsym (I) of 2.5. The completeness on high resolution (between 3.4 and 1.9) was 99.8 % with an Rsym (I) of 3.3. The unit cell parameters were a= 52.302 Å b= 58.490 Å and c= 106.036 Å, a=b=c=90°. The crystal was composed by one monomer per asymetric unit, has a solvent content of 52%, and one molecule per asymmetric unit (Mathews Volume = 2.57 Å<sup>3</sup> Da<sup>-1</sup>) The estimated B factor by Wilson plot is 29. Inspection of systematic absences along each axis indicated that the space group was orthorhombic P212121.

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	Table 1: Data Collection and Processing	
	Source	Grenoble ID14-3
	No of crytals	1
	Wavelength	0.93100 Å
5	Frames	331
	$\Delta\Phi$	1°
	Crystal to plate distance	260mm
	Time/frame	5sec(low res);20sec (high res)
	Number of Observations	28846
10	Data Reduction Program	HKL
	Unique reflections	26336
	Reflections Used	26331
	Resolution	30.0-1.9
	Completeness	100
15	Multiplicity	1
	Mosaicity	0.5
	aRsym .	3.6 % (15%)
	Space group	P212121
	a	52.302 Å
20	b	58.490 Å
	c	106.036 Å
	Wilson B-value	28.78 Å <sup>2</sup>

In the data collection, the last shell values are presented between parentheses.

# Structure Determination (Molecular Replacement)

The structure of the complex was solved by molecular replacement using the program AmoRe (Navaza, 1994) and the RARγ holo-LBD (Protein Data Bank accession code, 2lbd) as a search model. The top solution had a correlation coefficient of 27.8 ( next highest solution 26.2) and an R factor of 52.7 after AMoRe rigid-body refinement. A solution could also be found with RAR anta as a search model according to the following values: correlation coefficient of 21.4 ( next highest solution 19.8) and an R factor of 55.9.

## Table 2: Molecular Replacement Statistics

	Search Model:	••	holo-RARy
40	Program used		(PDB file 2LBD) AMoRe
	Resolution Range		15-3.0 Å
	Number of Reflections		4338
	Number of Atoms		2011
	RF Correlation (first solution)		18.8
45	TF Correlation (first solution)		24.3
	TF R-factor (first solution)		57.0
	Rigid Body Correlation		26.0
	Rigid Body R-factor		56.7

50 Structure Refinement

The automated model building Arp/wARP (Perrakis A. et al., 1999) combined with iterative structure refinement was used and permit us to obtain 3 chains constructed which correspond to 243 residues and a connectivity index of 0.98. The calculated electron density maps 3Fo-2Fc delivered Rcryst= 0.2703 and a Rfree = 0.2644.

A partial model of the monomer was build using the graphic program O (Jones et al., 1991) and subjected to alternating rounds of rigid body refinement with X-PLOR (Brünger, 1996) and manual building. The final steps, using cycles of positional

refinement, manual rebuilding, the torsion slow-cool procedure from the program X-PLOR, and individual isotropic B factor refinement delivered Rcryst = 0.2238 and a Rfree =0.2494. The final model refined at 1.9 Å, comprises 244 residues, one ligand, a peptide of 10 amino-acid residues, and 146 water molecules. According to Procheck (Laskowski et al., 1993) 93.2% of all residues in the model are in the most favoured main chain torsion angles Ramachandran regions, 5.9% in additional allowed regions, 0.4% in generously allowed regions and 0.4% are in disallowed regions. These last percentages corresponds to two residues (D403 and E404) situated in the loop 9-10, which did not present a well defined density.

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#### **Table 3: Final Refinement Parameters**

	Resolution Range	30.0-1.9	
	Reflections	26331	
15	R-factor	22.4%	
10			
	R-free	24.9%	
	# residues	201-452 (20)	7)
	# atoms	1977	1
•	RMS deviations		
20	bond lengths	0.008	
	bond angles	1.282	
	Average B-factors	•	
	Protein	29.5 Å <sup>2</sup>	
	Stearate	47.9 Å <sup>2</sup>	
25	Water	39.8 Å <sup>2</sup>	

#### Description of the Molecule

The structure of ROR\u00e3-LBD is complete from residues 208 through 451.

Analysis of the structure with program Procheck showed only minor exeptions to the allowed geometry. In the structure, the first seven residues of the chain (201-207) are 30 not seen in the electron density map and are probably disordered. This leaves only one residue before the initial residue of the first a-helix (H1) in the wild-type structure. On the C-terminal end, only the last residue (452) is not seen in the electron density map. The loop between helices H9 and H10 (residues N399 and E405) is not well defined.

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Folding and packing

As expected, the RORβ-LBD has the same overall three-dimensional structure as those of the other nuclear hormone receptor LBDs. The molecule is folded into a "helical sandwich" consisting of  $10 \alpha$ -helices. There are two small pieces of beta strand, forming a short beta sheet located in the core of the molecule between helices 5 and 6 near the ligand binding site. Helix 12 is folded toward the ligand binding domain core. Its last turn comes in close contact to H4, H11 and the co-activator peptide. An interaction surface comprising residues from the H3-H4 region and H12 allows the co-activator peptide to bind.

45 The following sequence of the peptide is seen in the crystal structure: HKILHRLLQE. The LXXLL motif also called the NR-box is included in an amphipathic α-helix interacting with a hydrophobic cleft on the LBD surface. In particularly, the side-chains of Leu 693 and Leu 694 are part of an hydrophobic cluster composed also by Val 274

(H3), Ile 292 (H4), and Leu 295 (H4).

The  $\gamma$  carboxylate of E448 (H12) forms hydrogen bonds with the backbone amides of 50 Leu 697 and Leu 698, residues of N-terminal turn of the peptide helix. This N-capping interaction was already described (Nolte & al., 1998, Shiau et al., 1998). This highly conserved glutamate residue is known to be important for transactivation. Another hydrogen bond requires Gln 288 (H4) OE2 with NE2 of His 695. The side chain of Glu 700 forms a water-mediated hydrogen bond to the carbonyl of residue Arg 696. 55

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### Binding of stearate

The volume of the ligand binding pocket is 758 Å<sup>3</sup>, which is close to that of VDR (660 Å<sup>3</sup>) (Rochel et al., 2000). A fortuitous ligand, stearic acid, was found in the ligand binding pocket, which was previously characterized by mass spectrometry. Thus, it appears that *E. coli*-endogeneous stearic acid was co-purified and co-crystallised with the heterologously expressed ROR $\beta$  LBD. The fatty acid (FA) is buried in a predominantly hydrophobic pocket formed by residues located in H3 (Gln 265, Ile 266, Ala269), H5 (Leu 300, Val303, Leu97), loop H5-H6 (Phe 113), H6 (Phe 320), and H7 (Leu131, Val338). Most of these residues make van der Waals contact with the aliphatic chain of the FA (Figure 3a). The cavity contains also 11 ordered water molecules. One oxygen atom of the carboxylate group forms hydrogen bond with NE2 of Gln265. This residue varies among ROR $\alpha$  and  $\beta$ . The other oxygen atom of the carboxylate group forms hydrogen bond with two ordered water molecules. These two molecules are part of a hydrogen bond network, which connects the carboxylate to other conserved residues among ROR $\alpha$  and  $\beta$  of the LBP namely Gln228 and Arg306. Stearate adopts a U-shaped conformation upon binding.

Table 4: Stearate contacts (3.5 Å)

20	Hydrogen bo	nds				
	O2	Gln 265 Nε2	2.79Å			
	O1	Wat 944		2.54Å O	Val 303	3.11Å
	Possible Clos	e Contacts				
25	O1	Ala 269 Cβ		3.31Å	•	
	O2	Gln 265 Cy		3.33Å		
	O2	Gln 265 Cδ		3:41Å		
	O2	Wat 946		3.06 Å		
	C3	Wat 944		3.43 Å		
30	C3	Wat 946		3.21 Å		
	C4	Wat 946		3.30 Å		
	C10	Phe 123 CE1	3.43 Å	5.5011		
	C11	Leu 131 CD2				

35 crystallization and structure determination of the RORβ LBD/ATRA (all-trans retinoic acid) complex

As mentioned above, the RORB LBD construct where the two C-terminal solventexposed cysteines have been removed by truncation of a 7-residue C-terminal segment has proved a valuable tool to get other crystal structures of the RORB LBD in complex 40 with other ligands. This is illustrated below with the description of the crystallization and the structure determination of the RORB LBD/ATRA (all-trans retinoic acid) complex. This new structure reveals another mode of binding for the ligand and suggests that natural and synthetic retinoids are candidate ligands for RORB. This family of compounds may thus be tested for binding to the RORB LBD, for instance by 45 mass spectrometry, and the crystallization may be tried in the positive cases. From the obtained structures, high-affinity ligands can be designed, synthetized, and tested in vivo, in vitro, as well as for crystallization. Even without the crystal structure of other complexes, filtering for ligand screening and/or design of better ligands can be achieved 50 through docking studies in computo.

Crystallization of the RORB LBD/ATRA complex

The RORβ LBD/ATRA complex was crystallized by vapor diffusion in the hanging-drop mode. The protein (the RORβ LBD containing stearic acid, purified as previously)
was co-crystallised with an excess ATRA and an excess SRC-1 (residues 686-700) under similar conditions as for the RORβ LBD/STE (stearic acid) complex. A 4 μl drop

was prepared by mixing 2  $\mu$ l of purified protein (5.8 mg/ml) with an equal volume of reservoir solution. The reservoir (500  $\mu$ l) contained 18% PEG 6000 and 100 mM Tris HCl pH=8.0. A crystal measuring 300x 160 x 100  $\mu$ m grew within 2 weeks at 22°C.

#### 5 Data Collection

The crystals were cryoprotected with a film of viscous paraffin oil and then flash frozen in liquid ethane at liquid nitrogen temperature. X-ray diffraction data were collected at liquid nitrogen temperature from a single frozen crystal at the BM14-CRG beamline at the ESRF Grenoble, France. Crystals diffracted X-rays to a resolution limit of 2.1 Å. All data were integrated and scaled using DENZO and SCALEPACK (Table 5). The data set between 20.0 and 2.1 Å shows a completeness of 100 % with an Rsym (I) of 4.5%. The completeness in the highest resolution shell (2.17-2.10 Å) was 100 % with an Rsym (I) of 17.5%. The unit cell parameters were a=52.199Å, b=58.125Å, and c=106.039Å, a=b=c=90°. The crystal contains one monomer per asymetric unit and a solvent content of 52%. The estimated B factor by Wilson plot is 32. Inspection of systematic absences along each axis indicated that the space group was P212121.

#### Structure Determination and Refinement

The structure of the complex was solved by molecular replacement using the RORβ LBD/STE complex as a starting model. The all-trans retinoic acid was built using Quanta (MSI). The final model (Rcryst = 0.2180 and Rfree =0.2549), refined at 2.1 Å (Table 5), comprises 244 residues from the RORβ LBD, 10 residues from the peptide, one ligand, and 139 water molecules. According to Procheck, 91.2% of all residues in the model are in the most favoured main chain torsion angles Ramachandran regions, 5.9% in additional allowed regions, 2.1% in generously allowed regions and 0.0% in disallowed regions.

### Binding of ATRA (all-trans retinoic acid)

The protein-ligand contacts within 3.5 Å are listed in Table 6. The present structure reveals the binding site for the carboxylate group of ATRA, which is hydrogen-bonded to Arg 306 and Arg 309 through a water molecule in each case (Figure 6). The binding mode is different from that of stearate (Figure 7), which is hydrogen-bonded to Gln 265 directly and to Gln 228 through a water molecule. On the other hand, stearate makes more Van der Waals contacts with pocket residues thanks to its flexible chain which assumes a U shape probably in order to maximize the number of such contacts. ATRA is more rigid, allowing less Van der Waals contacts. Thus, there seems to be a delicate balance between Van der Waals contacts and hydrogen bonds ligand binding to the RORβ LBD.

## 40 Table 5: Data collection and refinement statistics.

Source		ESRF BM14
Wavelength		0.976205 Å
Unique reflections		19431
Resolution range		20.0- 2.1
<sup>a</sup> Completeness		100 % (100 %)
Multiplicity Mosaicity		6.6 0.75°
<sup>a</sup> Rsym		4.5 % (17.5%)
Space group		P212121
a		52.199 Å
Ъ	air:	58.125 Å
c	r.	106.039 Å
	Wavelength Unique reflections Resolution range  aCompleteness Multiplicity Mosaicity  aRsym Space group a b	Wavelength Unique reflections Resolution range  aCompleteness Multiplicity Mosaicity  aRsym Space group a b

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<sup>a</sup>The last shell values are presented between parentheses.

	Resolution Range		20.0-2.1
	Reflections		17679
5	R-factor		21.8%
	R-free		25.5%
	# visible residues		244 (residues 208-451)
	# atoms		2219
	RMS deviations		
10	bond lengths		0.007
	bond angles		1.129
	Average B-factors		
	Protein and peptide		33.6 Å <sup>2</sup>
	All-trans retinoic acid	4.	40.3 Å <sup>2</sup>
15	Water		43.2 Å <sup>2</sup>
	Wilson B-factor		31.9 Å <sup>2</sup>

Table 6: ROR $\beta$  LBD/ATRA (all-trans retinoic acid) contacts within 3.5 Å

	Hydroge	en bonds N Gln 228	
	O1	N Gln 228	2.97 Å
	O1	Wat 802	2.72 Å
	O2	Wat 825	2.59 Å
25	NH1	Arg 306	2.92 Å
	NH1	Arg 309	2.84 Å
	Van der	Waals contacts	
	O1	Arg 306 Cδ	3.50 Å
30	O2	Tyr 229 N	3. <b>42</b> Å
	O2	Gln 228 N	3.42 Å
	C15	Gln 228 N	3.48 Å
	C15	Wat 825	3.39 Å
35	C18	Cys 262 Cβ	3.42 Å
	C18	Cys 262 Sy	3. <b>44</b> Å
	C19	Leu 319 O	3.34 Å
	C20	Wat 825	3.22 Å

Cell Culture and Transient Transfection Experiments.

HT22 were cultured in in Dulbecco's modified Eagle's medium (DMEM). The Medium was supplemented with 5% delipidated fetal calf serum, penicillin, streptomycin and glutamine. Transient transfection assays were carried out in 24-well plates (0.5 10<sup>5</sup> cells per well) N-[1-(2,3-dioleoyloxy)propyl]-N,N,N-trimethylammoniummethylsulfate (DOTAP) lipofection (Roche Molecular Biochemicals) according to the manufacturer's 45 protocol. Luciferase activity was assayed as recommended by the manufacturer (Promega) in a Microplate Luminometer (EG & G Berthold). Relative light units were

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normalized according to (Muller et al., 2002) and protein concentration was determined using the Bradford dye assay (Bio-Rad). All experiments were repeated at least five times.

Ligands. Purchased ligands include the following: all-trans-[20-methyl-3H]-retinoic acid (65 Ci/mmol) (NEN); all-trans-retinoic acid (Sigma)

Recombinant plasmids. Reporter plasmids. G5E1BTataLuc

Expression vectors. CMX-Gal, CMX-Gal-ROR\$201-459, pGEX-ROR\$201-459

described in (Greiner et al., 1996)

Ligand binding assays. Scintillation proximity assay were performed with purified bacterial expressed RORB-LBD (stehlin et al 2001) (250 ng per well) and all-trans-[20methyl-3H]-retinoic acid (60 Ci/mMol, NEN) in 96-well NiNTA-flash-plates (NEN) in a total volume of 100 µl. Binding buffer: 40 mM HEPES pH 7.6, 40 mM KCl, 0.2 % CHAPS, 0.1 mg/ml BSA. Binding was carried out for 1 hour at 4°C in 100 µl binding 15 buffer. Radioligand was diluted in binding buffer to a final concentration of 5 nM. Unlabelled competing ligands were serially diluted in binding buffer and added at final concentrations ranging from 1 nM to 10 µM. Plates were shaken at 25°C for 2 hours. Then the radioactivity was measured with a Packard Topcount at 2 min per well. All concentrations were assayed in triplicate and the results were averaged. Values from 20 wells void of competitor represented 100% binding. Saturation-binding experiments used the ligand concentrations indicated in the figure. Nonspecific binding was determined by including unlablled retinoic acid at 10<sup>4</sup> M and subtracted from total binding. Nonlinear regression analysis for the competition curves, saturation binding and Scratchard analysis to determine the Kd were performed using GRAPHPAD 25 PRISM.

Greiner, E. F., Kirfel, J., Greschik, H., Dorflinger, U., Becker, P., Mercep, A., and Schule, R. (1996). Functional analysis of retinoid Z receptor beta, a brain-specific nuclear orphan receptor. Proc Natl Acad Sci U S A 93, 10105-10110.

Muller, J. M., Metzger, E., Greschik, H., Bosserhoff, A. K., Mercep, L., Buettner, R., and Schule, R. (2002). The transcriptional coactivator FHL2 transmits Rho signals from the cell membrane into the nucleus. Embo J 21, 736-748.

TABLE A: Crystallographic Coordinates of RORbeta LBD/stearic acid/SRC1 peptide complex

40	3.0004	-							
ŦU	MOTA	1	CB	THR	208	14.051	-0.802	26.838	1.00 36.55
	MOTA	2	OG1	THR	208	15.478	-0.898	26.824	1.00 35.48
	ATOM	3	CG2	THR	208	13.533	-0.599	25.404	1.00 36.9%
	MOTA	4	С	THR	208	14.780	1.393	27.790	1.00 35.14
4 =	MOTA	5	0	THR	208	15.234	1.884	26.757	1.00 33.86
45	ATOM	6	N	THR	208	12.302	0.901	27.332	1.00 33.90
	ATOM	7	CA	THR	208	13.631	0.366	27.747	1.00 34.84
	ATOM	8	N	MET	209	15.261	1.697	28.997	1.00 35.20
	MOTA	9	CA	MET	209	16.358	2.647	29.169	1.00 34.91
Ε0	MOTA	10	CB	MET	209	16.717	2.770	30.658	1.00 34.61
50	MOTA	11	CG	MET	209	17.482	4.050	31.032	1.00 35.43
	MOTA	12	SD	MET	209	16.609	5.601	30.589	1.00 35.84
	MOTA	13	CE	MET	209	15.558	5.830	32.022	1.00 33.07
	ATOM	14	С	MET	209	17.598	2.235	28.346	1.00 34.50
	ATOM	15	0	MET	209	18.313	3.100	27.813	1.00 34.32
55	ATOM	16	N	SER	210	17.846	0.930	28.225	1.00 32.92
	ATOM	17	CA	SER	210	18.999	0.456	27.461	1.00 33.75
	ATOM	18	CB	SER	210	19.181	-1.064	27.604	1.00 34.40
	ATOM	19	OG	SER	210	18.057	-1.784	27.107	1.00 37.86
	ATOM	20	С	SER	210	18.886	0.821	25.983	1.00 37.56
60	ATOM	21	0	SER	210	19.888	1.145	25.345	1.00 32.59
	ATOM	22	N	GLU	211	17.684	0.746	25.422	1.00 32.55
	ATOM	23	CA	GLU	211	17.525	1.121	24.020	1.00 30.40
	MOTA	24	CB	GLU	211	16.125	0.782	23.484	1.00 30.37
	MOTA	25	CG	GLU	211	15.813	1.507	22.160	1.00 30.37
65	ATOM	26	CD	GLU	211	14.495	1.097	21.511	1.00 34.29
_	ATOM	27	OE1	GLU	211	13.563	0.690	22.233	1.00 34.29
	ATOM	28	OE2	GLU	211	14.384	1.205	20.267	1.00 34.73
						2504	2.203	20.207	1.00 34.73

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	ATOM ATOM	29 C GLU 30 O GLU	211	17.752 2.625 23.883 1.00 28.5 18.351 3.080 22.913 1.00 27.9
5	ATOM ATOM	31 N ILE 32 CA ILE		17.264 3.396 24.848 1.00 27.4 17.424 4.845 24.781 1.00 27.7
3	MOTA MOTA	33 CB ILE 34 CG2 ILE	212 212	16.764 5.571 25.978 1.00 26.3
	ATOM ATOM	35 CG1 ILE 36 CD1 ILE	212 212	15.257 5.276 26.029 1.00 26.50
10	MOTA MOTA	37 C ILE	212	18.895 5.226 24.757 1.00 27.70
	MOTA	39 N ASP	212 213	19.302 6.124 24.021 1.00 26.99 19.691 4.530 25.563 1.00 29.13
	ATOM ATOM	40 CA ASP 41 CB ASP	213 213	21.122 4.800 25.653 1.00 29.2 21.699 4.045 26.853 1.00 32.2
15	MOTA MOTA	42 CG ASP 43 OD1 ASP	213 213	23.083 4.517 27.233 1.00 34.55
	MOTA TOM	44 OD2 ASP 45 C ASP	213 213	24.004 3.674 27.248 1.00 37.52
	ATOM ATOM	46 O ASP 47 N ARG	213	22.804 5.137 23.954 1.00 27.10
20	ATOM ATOM	48 CA ARG	214 214	21.475 3.329 23.732 1.00 28.15 22.108 2.908 22.480 1.00 29.03
	MOTA	49 CB ARG 50 CG ARG	214 214	21.597 1.535 22.047 1.00 32.44 21.849 0.417 23.050 1.00 38.05
25	MOTA MOTA	51 CD ARG 52 NE ARG	214 214	21.039 -0.810 22.667 1.00 41.57
25	ATOM ATOM	53 CZ ARG 54 NH1 ARG	214 214	20.771 -3.082 23.582 1.00 49.23
	ATOM ATOM	55 NH2 ARG 56 C ARG	214 214	20.720 -3.894 24.632 1.00 50.33
30	ATOM ATOM	57 O ARG	214	21.785 3.928 21.383 1.00 27.33 22.624 4.236 20.543 1.00 26.60
	ATOM	59 CA ILE	215 215	20.559 4.446 21.391 1.00 26.45 20.150 5.432 20.395 1.00 24.84
	ATOM ATOM	60 CB ILE	215 215	18.629 5.699 20.472 1.00 26.20 18.280 7.043 19.821 1.00 25.14
35	ATOM ATOM	62 CG1 ILE 63 CD1 ILE	215 215	17.881 4.554 19.781 1.00 25.45
	ATOM ATOM	64 C ILE 65 O ILE	215 215	20.929 6.723 20.629 1.00 24.62
	ATOM ATOM	66 N ALA 67 CA ALA	216	21.050 7.116 21.893 1.00 24.39
40	ATOM ATOM	68 CB ALA	216 216	21.782 8.323 22.242 1.00 25.02 21.677 8.589 23.740 1.00 24.99
	MOTA	69 C ALA 70 O ALA	216 216	23.249 8.232 21.829 1.00 25.36 23.77\$ 9.151 21.193 1.00 25.93
45	ATOM ATOM	71 N GLN 72 CA GLN	217 217	23.922 7.137 22.177 1.00 25.23 25.332 6.999 21.819 1.00 26.24
40	ATOM ATOM	73 CB GLN 74 CG GLN	217 217	25.917 5.705 22.397 1.00 29.19
	ATOM ATOM	75 CD GLN 76 OE1 GLN	217 217	27.010 4.630 24.420 1.00 38.21
50	ATOM ATOM	77 NE2 GLN 78 C GLN	217 217	28.140 5.022 25.006 1.00 41.77
	ATOM ATOM	79 O GLN	217	25.556 7.041 20.305 1.00 25.19 26.518 7.651 19.823 1.00 24.32
	MOTA	81 CA ASN	218 218	24.659 6.392 19.568 1.00 23.86 24.725 6.341 18.113 1.00 23.77
55	MOTA MOTA	82 CB ASN 83 CG ASN	218 218	23.580 5.472 17.591 1.00 23.58 23.554 5.381 16.084 1.00 24.49
	ATOM ATOM	84 OD1 ASN 85 ND2 ASN	218 218	22.492 5.461 15.480 1.00 24.92
	ATOM ATOM	86 C ASN 87 O ASN	218 218	24.632 7.746 17.508 1.00 23.84
60	ATOM ATOM	88 N ILE 89 CA ILE	219 219	23.654 8.518 17.967 1.00 23.13
	ATOM ATOM	90 CB ILE	219	23.464 9.872 17.462 1.00 22.12 22.116 10.448 17.948 1.00 20.95
65	ATOM	92 CG1 ILE	219 219	22.033 11.927 17.630 1.00 18.97 20.975 9.653 17.300 1.00 20.42
05	ATOM ATOM	93 CD1 ILE 94 C ILE	219 219	19.602 9.904 17.878 1.00 21.20 24.615 10.784 17.874 1.00 22.86
	MOTA MOTA	95 O ILE 96 N ILE	219 220	25.132 11.552 17.063 1.00 21.51
70	ATOM ATOM	97 CA ILE 98 CB ILE	220 220	26.128 11.503 19.616 1.00 24.02
	ATOM ATOM	99 CG2 ILE	220	26.418 11.199 21.098 1.00 23.77 27.801 11.712 21.479 1.00 25.51
	ATOM	101 CD1 ILE	220 220	25.323 11.824 21.970 1.00 24.25 25.371 11.402 23.442 1.00 25.63
<i>7</i> 5	ATOM ATOM	102 C ILE 103 O ILE	220 220	27.379 11.217 18.783 1.00 24.51 28.076 12.133 18.338 1.00 24.01
	ATOM ATOM	104 N LYS 105 CA LYS	221 221	27.655 9.937 18.563 1.00 25.74
	ATOM ATOM	106 CB LYS 107 CG LYS	221 221	28.987 8.017 17.845 1.00 27.05
80	ATOM ATOM	108 CD LYS	221	30.218 5.948 17.211 1.00 33.17
	ATOM	110 NZ LYS	221 221	30.998 5.233 16.112 1.00 35.08 32.350 5.814 15.948 1.00 37.04
85	ATOM ATOM	111 C LYS 112 O LYS	221 221	28.724 10.027 16.352 1.00 26.19 29.710 10.504 15.783 1.00 26.37
00	ATOM ATOM	113 N SER 114 CA SER	222 222	27.538 9.932 15.765 1.00 24.31 27.365 10.388 14.389 1.00 24.58
				2.00 24.38

	ATOM	115 C	B SER	222	25	047	10 105	12 00'4	
	ATOM		G SER	222		.947	10.105	13.894	1.00 25.00
	MOTA	117 C		222		.818	10.539	12.544	1.00 27.88
	MOTA	118 0		222		.654	11.882	14.278	1.00 23.15
5	ATOM	110 N		222		.312	12.332	13.340	1.00 20.13
•	MOTA	120 C		223		.160	12.640	15.254	1.00 22.79
	ATOM			223		. 369	14.081	15.292	1.00 23.51
	ATOM			223		. 694	14.672	16.530	1.00 22.71
			G HIS	223		. 071	16.095	16.803	1.00 22.35
10	ATOM		D2 HIS	223		. 948	16.627	17.686	1.00 23.97
10	ATOM		D1 HIS	223		. 531	17.158	16.114	1.00 23.67
	MOTA		E1 HIS	223	27.	. 055	18.284	16.561	1.00 22.61
	ATOM		E2 HIS	223	27.	918	17.990	17.516	1.00 24.30
	ATOM	127 C	HIS	223	28.	860	14.408	15.334	1.00 24.83
16	ATOM	128 O	HIS	223	29.	348	15.233	14.570	1.00 23.29
15	MOTA	129 N	LEU	224	29.	581	13.758	16.239	1.00 26.00
	MOTA	130 C	A LEU	224	31.	005	14.012	16.378	1.00 27.42
	MOTA	131 C	B LEU	224		564	13.241	17.579	1.00 28.17
	MOTA	132 C		224	31.	065	13.762	18.936	1.00 29.44
	MOTA		D1 LEU	224		630	12.901	20.062	1.00 30.81
20	MOTA		D2 LEU	224		482	15.226		
	ATOM	135 C	LEU	224		791	13.686	19.118	1.00 31.36
	ATOM	136 0		224		777	14.358	15.116	1.00 27.94
	ATOM	137 N		225				14.823	1.00 28.46
	ATOM					352	12.676	14.366	1.00 26.53
25	ATOM			225		042	12.289	13.138	1.00 28.08
20	ATOM	139 CI		225		897	10.785	12.867	1.00 29.02
		140 C		225		994	9.881	14.083	1.00 32.55
	MOTA	141 CI		225		914	8.410	13.714	1.00 34.16
	ATOM		E1 GLU	225		093	8.046	12.822	1.00 35.71
20	ATOM		E2 GLU	225	32.	666	7.615	14.322	1.00 33.88
30	MOTA	144 C	GLU	225	31.	540	13.028	11.897	1.00 26.89
	MOTA	145 O	GLU	225	32.	105	12.862	10.820	1.00 27.36
	ATOM	146 N	THR	226	30.	499	13.845	12.032	1.00 26.42
	ATOM	147 C	A THR	226	29.	959	14.540	10.860	1.00 25.86
25	MOTA	148 C	3 THR	226	28.	574	13.972	10.486	1.00 24.69
35	MOTA	149 O	31 THR	226		670	14.165	11.579	1.00 21.37
	ATOM		32 THR	226		684	12.478	10.162	1.00 25.22
	MOTA	151 C	THR	226		850	16.067	10.890	
	ATOM	152 O	THR	226		016	16.645		1.00 26.84
	ATOM	153 N	CYS	227		670		10.196	1.00 25.61
40	ATOM	154 C		227			16.719	11.698	1.00 27.47
	ATOM	155 C		227		677	18.177	11.733	1.00 29.95
	MOTA	156 SC				725	18.694	13.160	1.00 30.26
	ATOM			227		129	18.666	13.964	1.00 31.37
	ATOM	157 C	CYS	227	31.		18.614	10.993	1.00 31.15
45		158 0	CYS	227	32.		17.926	11.044	1.00 32.10
10	ATOM	159 N	GLN	228	31.		19.737	10.291	1.00 32.99
	ATOM	160 C		228	33.		20.217	9.559	1.00 34.05
	ATOM	161 CE		228	32.		21.472	8.746	1.00 34.74
	ATOM	162 CG		228	33.		22.087	8.166	1.00 36.23
50	ATOM	163 CI		228	33.	732	23.051	7.040	1.00 36.08
JU	ATOM		El GLN	228	34.		23.216	6.172	1.00 37.80
	ATOM		E2 GLN	228	32.	579	23.710	7.049	1.00 35.92
	ATOM	166 C	GLN	228	34.	163	20.543	10.527	1.00 34.44
	ATOM	167 O	GLN	228	35.	345	20.276	10.254	1.00 35.97
	MOTA	168 N	TYR	229	33.	794	21.134	11.656	1.00 33.42
55	ATOM	169 CA	TYR	229	34.		21.508	12.664	1.00 34.12
	MOTA	170 CE	TYR	229	34.	804	23.025	12.814	1.00 34.64
	ATOM	171 CG		229	35.		23.753	11.578	1.00 35.84
	ATOM		1 TYR	229	36.		23.558	11.052	
	MOTA	173 CE		229	36.		24.278	9.925	1.00 37.22
60	MOTA	174 CD		229	34.		24.667		1.00 37.82
	ATOM	175 CE		229	34.		25.380	10.953	1.00 36.84
	ATOM	176 CZ		229	36.		25.191	9.841	1.00 37.23
	ATOM	177 OH		229				9.333	1.00 38.42
	ATOM				36.4		25.957	8.260	1.00 40.27
65	ATOM		TYR	229	34.4		20.895	14.004	1.00 34.39
		179 0	TYR	229	33.:		21.045	14.489	1.00 33.47
	ATOM	180 N	THR	230	35.3		20.202	14.601	1.00 35.45
	MOTA	181 CA		230	35.3	151	19.622	15.913	1.00 37.95
	ATOM	182 CB	THR	230	36.3	301	18.697	16.373	1.00 38.23
70	ATOM	183 OG	1 THR	230	37.9	502	19.463	16.518	1.00 40.39
70	MOTA	184 CG	2 THR	230	36.5	522	17.593	15.370	1.00 39.49
	MOTA	185 C	THR	230	35.6		20.807	16.851	1.00 38.40
	ATOM	186 0	THR	230	35.4		21.927	16.488	1.00 37.62
	MOTA	187 N	MET	231	34.5		20.567	18.049	
	ATOM	188 CA		231	34.4		21.614		1.00 40.09
75	ATOM	189 CB		231				19.055	1.00 42.13
. •	MOTA	190 CG			33.8		21.031	20.319	1.00 42.86
	ATOM			231	32.3		21.368	20.493	1.00 44.14
		191 SD		231	32.2		22.979	21.200	1.00 48.47
	ATOM	192 CE		231	31.4		23.899	19.813	1.00 44.81
80	MOTA	193 C	MET	231	35.7		22.239	19.392	1.00 42.66
OU	MOTA	194 0	MET	231	35.6		23.413	19.754	1.00 42.23
	ATOM	195 N	GLU	232	36.8		21.435	19.287	1.00 44.27
	MOTA	196 CA		232	38.1		21.900	19.564	1.00 46.03
	MOTA	197 CB		232	39.1		20.718	19.589	1.00 48.16
0.5	MOTA	198 CG		232	39.0		19.847	20.834	1.00 52.20
85	ATOM	199 CD		232	39.9		18.626	20.745	1.00 54.53
	ATOM		1 GLU	232	41.2		18.807	20.581	1.00 55.69
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	ATOM	201 OE2 GLU	232	39.452 17.483 20.831 1.00 55.83
	ATOM	202 C GLU	232	38.629 22.893 18.484 1.00 45.35
	ATOM ATOM	203 O GLU 204 N GLU	232 233	39.137 23.971 18.785 1.00 45.45
5	ATOM	205 CA GLU	233	38.449 22.506 17.227 1.00 44.58 38.837 23.341 16.099 1.00 43.02
	MOTA	206 CB GLU	233	38.530 22.625 14.780 1.00 43.47
	MOTA	207 CG GLU	233	39.477 21.486 14.414 1.00 43.69
	MOTA MOTA	208 CD GLU 209 OE1 GLU	233 233	39.053 20.792 13.134 1.00 44.50 37.937 20.228 13.113 1.00 42.94
10	ATOM	210 OE2 GLU	233	37.937 20.228 13.113 1.00 42.94 39.826 20.819 12.144 1.00 45.82
	MOTA	211 C GLU	233	38.130 24.693 16.128 1.00 42.63
	MOTA	212 O GLU	233	38.664 25.689 15.629 1.00 41.56
	ATOM ATOM	213 N LEU 214 CA LEU	234 234	36.927 24.716 16.702 1.00 41.55
15	ATOM	215 CB LEU	234	36.130 25.929 16.800 1.00 41.68 34.662 25.569 17.081 1.00 38.99
	MOTA	216 CG LEU	234	34.662 25.569 17.081 1.00 38.99 33.595 25.745 15.984 1.00 37.42
	ATOM	217 CD1 LEU	234	34.202 25.811 14.598 1.00 36.02
	ATOM	218 CD2 LEU	234	32.598 24.602 16.068 1.00 35.04
20	ATOM ATOM	219 C LEU 220 O LEU	234 234	36.659 26.884 17.874 1.00 43.02 36.689 28.097 17.665 1.00 42.82
	ATOM	221 N HIS	235	22 25
	ATOM	222 CA HIS	235	37.063 26.347 19.024 1.00 44.76 37.609 27.183 20.100 1.00 46.16
	MOTA	223 CB HIS	235	37.997 26.304 21.303 1.00 47.16
25	MOTA MOTA	224 CG HIS 225 CD2 HIS	235	36.823 25.826 22.102 1.00 47.88
	ATOM	226 ND1 HIS	235 235	35.624 26.405 22.363 1.00 48.26 36.816 24.615 22.765 1.00 48.61
	ATOM	227 CE1 HIS	235	25 554 24 457
	ATOM	. 228 NE2 HIS	235	34.922 25.536 23.169 1.00 48.08
.30	ATOM	229 C HIS	235	38.833 27.943 19.580 1.00 46.16
,50	ATOM ATOM	230 O HIS	235	39.093 29.086 19.972 1.00 46.99
	ATOM	231 N GLN 232 CA GLN	236 236	39.570 27.304 18.676 1.00 46.28 40.763 27.888 18.078 1.00 46.35
	ATOM	233 CB GLN	236	40.763 27.888 18.078 1.00 46.35 41.709 26.769 17.647 1.00 48.10
25	ATOM	234 CG GLN	236	42.314 26.013 18.819 1.00 50.88
35	ATOM	235 CD GLN	236	43.066 24.776 18.378 1.00 53.03
	MOTA MOTA	236 OE1 GLN 237 NE2 GLN	236	42.483 23.846 17.799 1.00 54.30
	ATOM	238 C GLN	236 236	44.368 24.750 18.651 1.00 53.30 40.469 28.804 16.882 1.00 45.38
40	ATOM	239 O GLN	236	40.469 28.804 16.882 1.00 45.38 41.358 29.510 16.401 1.00 45.98
40	MOTA	240 N LEU	237	39.231 28.793 16.396 1.00 43.26
	ATOM ATOM	241 CA LEU	237	38.864 29.650 15.276 1.00 41.13
	ATOM	242 CB LEU 243 CG LEU	237 237	38.032 28.877 14.249 1.00 40.63 38.733 27.918 13.291 1.00 40.27
4	ATOM	244 CD1 LEU	237	27 700
45	MOTA	245 CD2 LEU	237	37.700 27.272 12.379 1.00 39.92 39.777 28.674 12.485 1.00 40.45
	MOTA	246 C LEU	237	38.081 30.878 15.727 1.00 39.51
	MOTA MOTA	247 O LEU 248 N ALA	237	38.086 31.903 15.047 1.00 38.80
	ATOM	248 N ALA 249 CA ALA	238 238	37.427 30.778 16.880 1.00 39.51 36.618 31.871 17.406 1.00 38.91
50	MOTA	250 CB ALA	238	36.618 31.871 17.406 1.00 38.91 35.908 31.423 18.694 1.00 39.73
	ATOM	251 C ALA	238	37.408 33.152 17.656 1.00 38.89
	ATOM ATOM	252 O ALA	238	36.832 34.239 17.716 1.00 38.65
	ATOM	253 N TRP 254 CA TRP	239 239	38.725 33.041 17.794 1.00 39.18 39.524 34.239 18.022 1.00 39.10
55	ATOM	255 CB TRP	239	39.524 34.239 18.022 1.00 39.10 40.771 33.912 18.844 1.00 39.97
	ATOM	256 CG TRP	239	40.439 33.575 20.265 1.00 41.05
	ATOM	257 CD2 TRP	239	40.329 34.502 21.357 1.00 41.89
	ATOM ATOM	258 CE2 TRP 259 CE3 TRP	239	39.925 33.764 22.496 1.00 42.28
60	ATOM	260 CD1 TRP	239 239	40.527 35.889 21.481 1.00 42.04 40.111 32.345 20.768 1.00 41.20
	ATOM	261 NE1 TRP	239	39.800 32.451 22.113 1.00 41.62
	ATOM	262 CZ2 TRP	239	39.718 34.369 23.749 1.00 42.42
	ATOM ATOM	263 CZ3 TRP 264 CH2 TRP	239	40.318 36.495 22.734 1.00 41.71
65	ATOM	264 CH2 TRP 265 C TRP	239 239	39.917 35.732 23.846 1.00 41.59 39.904 34.917 16.715 1.00 38.66
	ATOM	266 O TRP	239	39.904 34.917 16.715 1.00 38.66 40.315 36.081 16.708 1.00 39.17
	MOTA	267 N GLN	240	39.750 34.191 15.613 1.00 37.88
	ATOM	268 CA GLN	240	40.052 34.715 14.281 1.00 38.38
70	ATOM ATOM	269 CB GLN 270 CG GLN	240	40.402 33.569 13.325 1.00 39.13
, 0	ATOM	271 CD GLN	240 240	41.815 33.009 13.448 1.00 43.03 42.865 33.999 12.962 1.00 45 47
	ATOM	272 OE1 GLN	240	42.865 33.999 12.962 1.00 45.47 42.697 34.640 11.913 1.00 46.02
	MOTA	273 NE2 GLN	240	43.962 34.121 13.712 1.00 45.97
<i>7</i> 5	ATOM	274 C GLN	240	38.841 35.473 13.726 1.00 38.04
75	ATOM ATOM	275 O GLN	240	37.750 34.900 13.590 1.00 36.35
	ATOM	276 N THR 277 CA THR	241 241	39.029 36.752 13.406 1.00 37.28
	ATOM	278 CB THR	241	37.938 37.554 12.865 1.00 37.13 37.417 38.596 13.901 1.00 38.89
on	ATOM	279 OG1 THR	241	38.436 39.565 14.186 1.00 40.81
80	ATOM	280 CG2 THR	241	37.028 37.907 15.208 1.00 39.48
	ATOM ATOM	281 C THR 282 O THR	241	38.347 38.279 11.580 1.00 36.22
	ATOM	282 O THR 283 N HIS	241 242	39.485 38.758 11.451 1.00 36.33 37.430 38.324 10.613 1.00 34.05
or.	ATOM	284 CA HIS	242	37.430 38.324 10.613 1.00 34.05 37.695 39.012 9.354 1.00 31.44
85	MOTA	285 CB HIS	242	36.472 38.974 8.436 1.00 29.25
	ATOM	286 CG HIS	242	36.149 37.615 7.904 1.00 27.92

•	MOTA	287 CD2 HIS	242	36 71" 36 007		
				36.887 څ.73	6.915	1.00 26.55
	MOTA	288 ND1 HIS	242	35.111 36.853	8.393	1.00 27.30
	MOTA	289 CE1 HIS	242	35.055 35.715	7.727	1.00 26.17
_	ATOM	290 NE2 HIS	242	36.020 35.710		
5	ATOM	291 C HIS			6.826	1.00 27.22
0			242	38.020 40.465	9.668	1.00 30.68
	ATOM	292 O HIS	242	37.358 41.096	10.490	1.00 30.78
	MOTA	293 N THR	243	39.038 40.991	9.004	
	MOTA	294 CA THR	243			1.00 31.03
				39.460 42.372	9.199	1.00 30.79
10	ATOM	295 CB THR	243	40.822 42.612	8.543	1.00 30.73
10	MOTA	296 OG1 THR	243	40.717 42.383	7.126	
	MOTA	297 CG2 THR	243			1.00 31.15
				41.864 41.669	9.140	1.00 29.69
	MOTA	298 C THR	243	38.470 43.363	8.595	1.00 31.03
	MOTA	299 O THR	243	37.534 42.970	7.901	
	MOTA	300 N TYR	244			1.00 29.40
15				38.684 44.648	8.868	1.00 31.19
10	MOTA	301 CA TYR	244	37.834 45.702	8.324	1.00 31.95
	ATOM	302 CB TYR	244	38.297 47.095	8.802	
	MOTA	303 CG TYR	244			1.00 33.18
				37.829 47.457	10.204	1.00 33.91
	MOTA	304 CD1 TYR	244	38.719 47.484	11.289	1.00 35.00
00	MOTA	305 CE1 TYR	244	38.268 47.784	12.599	1.00 35.72
20	MOTA	306 CD2 TYR	244	36.486 47.736		
	MOTA				10.450	1.00 35.64
		307 CE2 TYR	244	36.025 48.032	11.740	1.00 35.81
	MOTA	308 CZ TYR	244	36.915 48.054	12.809	1.00 36.54
	ATOM	309 OH TYR	244	36.440 48.350		
	ATOM				14.072	1.00 36.95
25			244	37.894 45.641	6.805	1.00 31.62
20	MOTA	311 O TYR	244	36.879 45.842	6.123	1.00 31.91
	ATOM	312 N GLU	245	39.085 45.363	6.280	
	ATOM					1.00 30.27
			245	39.281 45.271	4.841	1.00 30.86
	MOTA	314 CB GLU	245	40.764 45.070	4.502	1.00 32.11
	ATOM	315 CG GLU	245	41.664 46.274		
30	MOTA				4.773	1.00 34.84
			245	41.999 46.477.	6.248	1.00 36.73
	MOTA	317 OE1 GLU	245	42.570 47.548	6.573	1.00 37.44
	ATOM	318 OE2 GLU	245	41.710 45.578		
	ATOM				7.080	1.00 36.51
			245	38.476 44.105	4.283	1.00 29.31
25	MOTA	320 O GLU	245	37.722 44.262	3.325	1.00 28.06
35	ATOM	321 N GLU	246	38.632 42.939		
			_		4.904	1.00 28.59
	MOTA	322 CA GLU	246	37.921 41.740	4.458	1.00 28.73
	MOTA	323 CB GLU	246	38.360 40.539	5.298	1.00 28.89
	MOTA	324 CG GLU	246	39.841 40.230		
					5.106	1.00 33.43
<b>4</b> 0	ATOM	325 CD GLU	246	40.377 39.192	6.065	1.00 34.90
40	ATOM	326 OE1 GLU	246	40.008 39.213	7.259	1.00 36.44
	MOTA	327 OE2 GLU	246	41.196 38.363		
	ATOM				5.625	1.00 37.65
			246	36.407 41.941	4.515	1.00 26.90
	MOTA	329 O GLU	246	35.690 41.539	3.604	1.00 26.66
	MOTA	330 N ILE	247			
45					5.575	1.00 27.96
40	ATOM	331 CA ILE	247	34.488 42.838	5.702	1.00 26.28
	ATOM	332 CB ILE	247	34.155 43.539	7.048	1.00 26.69
	ATOM	333 CG2 ILE	247			
				32.729 44.062	7.031	1.00 25.56
	MOTA	334 CG1 ILĖ	247	34.360 42.570	8.222	1.00 25.48
	ATOM	335 CD1 ILE	247	33.500 41.318	8.148	1.00 26.47
50	MOTA	336 C ILE	247			
	ATOM				4.546	1.00 27.42
		337 O ILE	247	32.977 43.544	3.954	1.00 25.31
	MOTA	338 N LYS	248	34.876 44.723	4.214	1.00 27.71
	ATOM	339 CA LYS	248			
				34.538 45.638	3.135	1.00 28.31
==	MOTA	340 CB LYS	248	35.547 46.786	3.059	1.00 31.00
55	ATOM	341 CG LYS	248	34.912 48.072	2.556	1.00 36.20
	MOTA	342 CD LYS	248			
	ATOM				3.708	1.00 37.72
		343 CE LYS	248	33.507 47.965	4.691	1.00 39.77
	ATOM	344 NZ LYS	248	32.922 48.683	5.861	1.00 40.50
	MOTA	345 C LYS	248	_		
60	ATOM		240		1.802	1.00 27.15
00			248	33.618 45.191	0.972	1.00 25.35
	ATOM	347 N ALA	249	35.404 43.976	1.612	1 00 27.48
	ATOM	348 CA ALA	249	35.462 43.197	0.380	
	MOTA	349 CB ALA				1.00 27.44
			249	36.639 42.235	0.423	1.00 28.05
<b>/</b> F	ATOM	350 C ALA	249	34.151 42.427	0.213	1.00 27.33
65	MOTA	351 O ALA	249	33.576 42.386	-0.882	
	ATOM					1.00 26.70
			250	33.681 41.820	1.303	1.00 26.77
	ATOM	353 CA TYR	250	32.428 41.072	1.272	1.00 26.29
	ATOM	354 CB TYR	250	32.131 40.421		
	ATOM				2.628	1.00 26.30
70		355 CG TYR	250	32.869 39.129	2.881	1.00 26.73
<i>7</i> 0	ATOM	356 CD1 TYR	250	32.749 38.051	2.008	1.00 26.93
	ATOM	357 CE1 TYR	250			
	ATOM					1.00 27.90
		358 CD2 TYR	250	33.674 38.981	4.007	1.00 27.33
	ATOM	359 CE2 TYR	250	34.342 37.788		1.00 27.78
	ATOM					
<i>7</i> 5			250	34.210 36.731		1.00 27.25
, 5	ATOM	361 OH TYR	250	34.878 35.556	3.650	1.00 28.52
	ATOM	362 C TYR	250	31.276 41.997		
	ATOM					1.00 25.31
		363 O TYR	250	30.352 41.612	0.230	1.00 24.79
	ATOM	364 N GLN	251	31.324 43.213		1.00 26.05
• •	ATOM	365 CA GLN	251	30.261 44.169		
80						1.00 27.36
00	ATOM	366 CB GLN	251	30.311 45.309	2.208	1.00 28.26
	MOTA	367 CG GLN	251	30.146 44.860		1.00 29.79
	ATOM	368 CD GLN	251			
						1.00 32.00
	ATOM	369 OE1 GLN	251	30.908 46.963	4.465	1.00 33.43
0.5	ATOM	370 NE2 GLN	251	29.208 45.972		1.00 30.11
85	ATOM	371 C GLN	251	30.333 44.739		
						1.00 28.15
	ATOM	372 O GLN	251	29.348 45.278	-0.714	1.00 28.35

	ATOM	277	M	CDD	252				
	ATOM	373 374	N CA	SER SER	252 252	31.4: 31.6			1.00 28.46
	ATOM	375	CB	SER	252	33.1			1.00 29.58 1.00 29.66
5	ATOM	376	OG	SER	252	33.3			1.00 23.66
3	MOTA MOTA	377	C	SER	252	31.2		-3.225	1.00 30.02
	ATOM	378 379	O N	SER Lys	252 253	31.3; 30.9;		_	1.00 30.26
	ATOM	380	CA	LYS	253	30.5			1.00 29.52
10	ATOM	381	СВ	LYS	253	30.4			1.00 30.07 1.00 30.99
10	ATOM	382	CG	LYS	253	31.79		-2.457	1.00 33.63
	ATOM ATOM	383 384	CD	LYS LYS	253 253	32.60		-3.697	1.00 35.38
	ATOM	385	NZ	LYS	253	33.91 33.69		-3.352 -2.761	1.00 38.01
15	ATOM	386	С	LYS	253	29.15		-4.250	1.00 36.66 1.00 29.23
15	ATOM	387	0	LYS	253	28.33	3 42.815	-3.663	1.00 29.23
	ATOM ATOM	388 389	N CA	SER SER	254	28.92		-5.446	1.00 29.17
	MOTA	390	CB	SER	254 254	27.63 27.66		-6.080 -7.545	1.00 29.19
20	ATOM	391	ŌĞ	SER	254	27.81		-7.640	1.00 29.22 1.00 25.88
20	ATOM	392	Ç	SER	254	26.71		-5.341	1.00 29.60
	MOTA	393	0	SER	254	27.17		-4.739	1.00 29.62
	MOTA MOTA	394 395	N CA	ARG ARG	255 255	25.41 24.43		-5.404	1.00 28.75
	ATOM	396	CB	ARG	255	23.03		-4.749 -4.969	1.00 29.78
25	ATOM	397	CG	ARG	255	21.94		-4.139	1.00 31.17 1.00 34.14
	ATOM	398	CD	ARG	255	20.77	3 41.191	-3.965	1.00 37.49
	ATOM ATOM	399 400	NE	ARG	255	19.50		-3.868	1.00 40.31
	ATOM	401	CZ	ARG ARG	255 255	19.10 19.89		-4.755	1.00 41.60
30	ATOM	402		ARG	255	17.92		-5.782 -4.631	1.00 44.13 1.00 39.96
	ATOM	403	C	ARG	255	24.50		-5.255	1.00 39,96 1.00 27.97
	ATOM	404	0	ARG	255	24.37		-4.473	1.00 27.13
	ATOM ATOM	405 406	N CA	GLU	256 256	24.74 24.85		-6.549	1.00 27.81
35	ATOM	407	CB	GLU	256	24.87		-7.115 -8.647	1.00 28.27
	MOTA	408	CG	GLU	256	24.02		-9.243	1.00 29.71 1.00 34.67
	ATOM	409	CD	GLU	256	24.70		-9.149	1.00 34.34
	ATOM ATOM	410 411	OE1	GLU	256 256	25.74		-9.808	1.00 37.48
40	ATOM	412	C	GLU	256	24.19 26.12		-8.417 -6.639	1.00 34.93
	MOTA	413	0	GLU	256	26.10		-6.379	1.00 27.13 1.00 26.34
	ATOM	414	N	ALA	257	27.22	1, 37.322	-6.543	1.00 26.59
	MOTA MOTA	415 416	CA CB	ALA ALA	257	28.49		-6.108	1.00 24.46
45	ATOM	417	C	ALA	257 257	29.59 28.40		-6.190	1.00 23.06
	ATOM	418	ŏ	ALA	257	28.82		-4.685 -4.413	1.00 23.27 1.00 22.83
	ATOM	419	N	LEU	258	27.85		-3.780	1.00 22.28
	ATOM ATOM	420 421	CA	LEU	258	27.74		-2.386	1.00 22.36
50	ATOM	422	CB CG	LEU	258 258	27.38 27.62		-1.480	1.00 21.42
	ATOM	423		LEU	258	29.10		0.012 0.264	1.00 21.16 1.00 22.80
	MOTA	424	CD2	LEU	258	27.09		0.857	1.00 22.80
	ATOM ATOM	425	Ç	LEU	258	26.71		-2.253	1.00 22.29
55	ATOM	426 427	O N	LEU TRP	258 259	26.923 25.608		-1.498	1.00 21.82
	ATOM	428	CA	TRP	259	24.61		-2.990 -2.921	1.00 21.90 1.00 23.48
	ATOM	429	CB	TRP	259	23.40		-3.823	1.00 24.84
	ATOM	430	CG	TRP	259	22.26	35.370	-3.052	1.00 28.57
60	ATOM ATOM	431 432	CD2	TRP TRP	259 259	21.329 20.509		-2.259	1.00 30.31
	ATOM	433		TRP	259	21.10		-1.594 -2.039	1.00 31.88
	MOTA	434		TRP	259	21.97		-2.853	1.00 31.88
	ATOM	435		TRP	259	20.92	36.826	-1.977	1.00 31.45
65	MOTA MOTA	436 437	CZ2 CZ3	TRP TRP	259 259	19.484		-0.721	1.00 33.37
	ATOM	438	CH2	TRP	259	20.084 19.288		-1.171	1.00 32.58
	ATOM	439	C	TRP	259	25.279		-0.520 -3.328	1.00 33.41 1.00 23.16
	ATOM	440	0	TRP	259	25.066		-2.695	1.00 23.39
70	ATOM .	441 442	N	GLN	260	26.094		-4.378	1.00 24.68
, 0	ATOM	443	CA CB	GLN GLN	260 260	26.793 27.666		-4.824	1.00 24.94
	ATOM	444	CG	GLN	260	28.451		-6.046 -6.568	1.00 28.06 1.00 34.11
	ATOM	445	CD	GLN	260	29.968		-6.467	1.00 38.33
<i>7</i> 5	ATOM	446	OE1	GLN	260	30.524	31.565	-5.390	1.00 39.00
75	ATOM ATOM	447	NE2	GLN	260	30.650		-7.594	1.00 40.25
	ATOM	448 449	0	GLN GLN	260 260	27.671 27.671		-3.695	1.00 24.10
	ATOM	450	Ŋ	GLN	261	28.429		-3.435 -3.037	1.00 23.36 1.00 22.77
80	MOTA	451	CA	GLN	261	29.302	31.926	-1.940	1.00 23.59
80	ATOM	452	CB	GLN	261	30.089		-1.395	1.00 25.53
	ATOM ATOM	453 454	CG CD	GLN GLN	261 261	31.165 31.847		-2.321	1.00 31.43
	ATOM	455	OE1		261	31.616		-1.754 -2.226	1.00 35.45 1.00 38.71
0=	MOTA	456	NE2	GLN	261	32.678		-0.733	1.00 33.46
85	MOTA	457	C	GLN	261	28.508	31.295	-0.796	1.00 22.79
	ATOM	458	0	GLN	261	28.893	30.254	-0.255	1.00 21.63

	ATOM	459	N C	YS 262	27.404	31.940	-0.425	1.00 21.36
	ATOM	460	_	YS 262	26.558	31.437	0.651	1.00 21.18
	ATOM	461		YS 262	25.483	32.453	1.003	1.00 20.56
	ATOM	462		YS 262	26.149	33.886	1.830	
5	ATOM	463		YS 262	25.907	30.110		1.00 23.42
9							0.287	1.00 20.19
	ATOM	464			25.800	29.216	1.128	1.00 20.82
	ATOM	465		LA 263	25.475	29.977	-0.962	1.00 19.51
	MOTA	466		LA 263	24.855	28.731	-1.391	1.00 20.19
10	ATOM	467		LA 263	24.323	28.875	-2.790	1.00 19.19
10	MOTA	468		LA 263	25.871	27.582	-1.319	1.00 20.32
	MOTA	469	OA	LA 263	25.530	26 455	-0.946	1.00 20.47
	ATOM	470	N I	LE 264	27.120	27.869	-1.666	1.00 19.64
	ATOM	471	CA I	LE 264	28.163	26.844	-1.613	1.00 20.56
	MOTA	472	CB I	LE 264	29.479	27.352	-2.233	1.00 21.64
15	MOTA	473	CG2 I	LE 264	30.599	26.336	-2.003	1.00 24.40
	MOTA	474	CG1 I		29.276	27.584	-3.733	1.00 22.79
	ATOM	475	CD1 I		30.506	28.182	-4.453	1.00 23.68
	ATOM	476		LE 264	28.411	26.426	-0.169	1.00 19.92
	MOTA	477		LE 264	28.490	25.235	0.142	1.00 20.57
20								
20	ATOM	478		LN 265	28.518	27.408	0.720	1.00 20.33
	MOTA	479		LN 265	28.749	27.108	2.122	1.00 20.30
	MOTA	480		LN 265	28.961	28.392	2.919	1.00 22.53
	MOTA	481		LN 265	29.345	28.128	4.349	1.00 27.06
25	MOTA	482		LN 265	30.391	27.024	4.480	1.00 30.59
25	ATOM	483	OE1 G	LN 265	31.470	27.086	3.866	1.00 31.46
	MOTA	484	NE2 G	LN 265	30.075	26.003	5.286	1.00 31.02
	MOTA	485	C G	LN 265	27.584	26.313	2.722	1.00 19.48
	ATOM	486	0 G	LN 265	27.800	25.335	3.435	1.00 18.61
	ATOM	487		LE 266	26.357	26.734	2.427	1.00 18.19
30	ATOM	488		LE 266	25.167	26.049		1.00 19.33
	ATOM	489		LE 266	23.877	26.775	2.494	1.00 19.84
	ATOM	490	CG2 I		22.652	25.925	2.813	1.00 17.56
	ATOM	491	CG1 I		23.797	28.134		1.00 20.35
			CD1 I			28.987	3.179	
35	ATOM	492			22.643		2.693	1.00 21.92
55	ATOM	493		LE 266	25.137	24.619	2.406	1.00 19.49
	ATOM	494		LE 266	24.860	23.681	3.151	1.00 19.71
	ATOM	495		HR 267	25.427	24.452	1.120	1.00 19.07
	MOTA	496		HR 267	25.426	23.117	0.529	1.00 20.39
40	MOTA	497		HR 267	25.732	23.173	-0.973	1.00 19.62
40	ATOM	498	OG1 T	HR 267	24.727	23.949	-1.624	1.00 18.77
	MOTA	499	CG2 T	HR 267	25.747	21.767	-1.577	1.00 19.77
	ATOM	500	C T	HR 267	26.476	22.239	1.204	1.00 19.70
	ATOM	501	ОТ	HR 267	26.240	21.063	1.484	1.00 19.00
	MOTA	502	N H	IS 268	27.642	22.823	1.449	1.00 18.99
45	MOTA	503	CA H	IS 268	28.734	22.113	2.098	1.00 19.17
	ATOM	504		IS 268	29.926	23.063	2.248	1.00 20.12
	MOTA	505		IS 268	31.167	22.409	2.764	1.00 22.30
	ATOM	506	CD2 H		32.052	22.803	3.707	1.00 24.34
	ATOM	507	ND1 H		31.634	21.207	2.279	1.00 24.49
50	ATOM	508	CE1 H		32.752	20.887	2.903	1.00 23.24
-	ATOM	509	NE2 H		33.029	21.838	3.775	1.00 23.14
	ATOM	510		IS 268	28.237	21.616	3.462	1.00 19.37
	ATOM	511		IS 268	28.415	20.449	3.811	1.00 19.15
	MOTA	512		LA 269	27.587	22.501	4.215	1.00 17.47
55						22.139		
55	ATOM ATOM	513			27.050		5.525	1.00 18.95
		514		LA 269	26.522	23.380	6.237	1.00 18.60
	MOTA	515		LA 269	25.938	21.090	5.406	1.00 18.49
	MOTA	516		LA 269	25.838	20.181	6.229	1.00 19.32
4٥	ATOM	517		LE 270	25.104		4.377	1.00 17.85
60	ATOM	518		LE 270	24.017	20.277	4.165	1.00 17.94
	ATOM	519		LE 270	23.113	20.735	2.999	1.00 17.72
	ATOM	520		LE 270	22.238	19.569	2.502	1.00 15.68
•	ATOM	521	CG1 I		22.256	21.914	3.476	1.00 17.69
<b>/-</b>	ATOM	522	CD1 I	LE 270	21.442	22.593	2.381	1.00 19.17
65	MOTA	523	C I	LE 270	24.571	18.883	3.889	1.00 19.48
	ATOM	524	0 1	LE 270	24.049	17.881	4.377	1.00 17.18
	MOTA	525		LN 271	25.644	18.815	3.114	1.00 19.72
	ATOM	526		LN 271	26.229	17.519	2.826	1.00 20.49
	ATOM	527		LN 271	27.376	17.687	1.827	1.00 21.65
70	ATOM	528		LN 271	26.832	18.047	0.439	1.00 22.49
, 0	ATOM	529		LN 271	27.895	18.166	-0.646	1.00 23.92
	ATOM	530	OE1 G		27.588	18.037	-1.831	1.00 26.25
	ATOM				29.129			
		531	NE2 G			18.429	-0.252	1.00 23.47
<i>7</i> 5	ATOM	532		LN 271	26.663	16.804	4.118	1.00 20.60
, ,	ATOM	533		LN 271	26.516	15.586	4.236	1.00 20.59
	ATOM	534		YR 272	27.159	17.552	5.098	1.00 20.89
	ATOM	535		YR 272	27.547	16.940	6.368	1.00 21.15
	ATOM	536		YR 272	28.329	17.933	7.231	1.00 23.11
00	MOTA	537		YR 272	29.801	18.001	6.871	1.00 26.45
80	ATOM	538	CD1 T	YR 272	30.637	16.898	7.065	1.00 29.06
	ATOM	539		YR 272	31.989	16.937	6.702	1.00 31.21
	ATOM	540		YR 272	30.351	19.153	6.306	1.00 28.01
				YR 272	31.705	19.203	5.938	1.00 30.00
		541	CEZ I					1.00 30.00
_	MOTA	541 542			32.513	18.091		1.00 31.38
85	ATOM ATOM	542	CZ T	YR 272		18.091 18.137	6.140 5.786	
85	MOTA		CZ T OH T		32.512 33.846 26.312		6.140	1.00 31.38

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	ATOM	545 O TYR	272	26.378	15.401	7.810	1.00 20.19
	ATOM	546 N VAL	273	25.185	17.122	6.973	1.00 18.53
	ATOM ATOM	547 CA VAL 548 CB VAL	273 273	23.950	16.687	7.623	1.00 18.96
5	ATOM	549 CG1 VAL	273	22.832 21.529	17.740 17.186	7.496 8.052	1.00 18.38 1.00 15.65
	ATOM	550 CG2 VAL	273	23.229	19.004	8.247	1.00 17.10
	ATOM ATOM	551 C VAL 552 O VAL	273	23.474	15.365	7.007	1.00 19.57
	ATOM	553 N VAL	273 274	22.881 23.731	14.526 15.181	7.687 5.718	1.00 20.30 1.00 19.26
10	ATOM	554 CA VAL	274	23.352	13.934	5.065	1.00 19.26
	ATOM ATOM	555 CB VAL 556 CG1 VAL	274	23.595	13.997	3.538	1.00 19.96
	ATOM	557 CG2 VAL	274 274	23.323 22.678	12.640 15.052	2.914 2.905	1.00 22.18
15	MOTA	558 C VAL	274	24.191	12.808	5.685	1.00 20.72 1.00 21.11
15	MOTA MOTA	559 O VAL 560 N GLU	274	23.668	11.746	6.021	1.00 22.06
	MOTA	561 CA GLU	275 275	25.487 26.401	13.062 12.088	5.854 6.446	1.00 22.26 1.00 23.73
	MOTA	562 CB GLU	275	27.836	12.632	6.449	1.00 26.76
20	ATOM ATOM	563 CG GLU 564 CD GLU	275	28.448	12.827	5.058	1.00 30.97
	ATOM	565 OE1 GLU	275 275	29.000 28.264	11.534 10.512	4.446	1.00 34.75 1.00 34.78
	MOTA	566 OE2 GLU	275	30.180	11.553	3.995	1.00 34.78
	MOTA MOTA	567 C GLU 568 O GLU	275	25.954	11.803	7.875	1.00 22.91
25	ATOM	568 O GLU 569 N PHE	275 276	26.046 25.468	10.674 12.842	8.354 8.547	1.00 21.80
	ATOM	570 CA PHE	276	24.978	12.725	9.915	1.00 21.94 1.00 21.89
	ATOM ATOM	571 CB PHE 572 CG PHE	276	24.512	14.101	10.412	1.00 20.02
• •	ATOM	572 CG PHE 573 CD1 PHE	276 276	23.891 24.507	14.091 13.431	11.790	1.00 20.99
30	ATOM	574 CD2 PHE	276	22.722	14.817	12.850 12.040	1.00 20.12 1.00 20.12
	ATOM ATOM	575 CE1 PHE 576 CE2 PHE	276	23.975	13.502	14.144	1.00 21.36
	ATOM	576 CE2 PHE 577 CZ PHE	276 276	22.182 22.808	14.895	13.325 14.381	1.00 20.21
25	MOTA	578 C PHB	276	23.809	11.741	9.935	1.00 19.91 1.00 21.78
35	ATOM ATOM	579 O PHE 580 N ALA	276	23.815	10.771	10.688	1.00 22.96
	ATOM	580 N ALA 581 CA ALA	277 277	22.813 21.626	11.997 11.148	9.091	1.00 21.26
	ATOM	582 CB ALA	277	20.650	11.705	9.012 7.979	1.00 21.02 1.00 19.08
40	ATOM ATOM	583 C ALA 584 O ALA	277	21.968	9.700	8.671	1.00 21.78
10	ATOM	584 O ALA 585 N LYS	277 278	21.450 22.836	8.774 9.511	9.294	1.00 22.63
	MOTA	586 CA LYS	278	23.240	8.173	7.683 7.256	1.00 23.13 1.00 25.28
	ATOM ATOM	587 CB LYS 588 CG LYS	278	24.209	8.275	6.078	1.00 24.01
45	ATOM	588 CG LYS 589 CD LYS	278 278	23.561 24.575	8.837 8.997	4.803	1.00 26.41
	ATOM	590 CE LYS	278	25.265	7.676	3.689 3.395	1.00 24.85 1.00 25.80
	ATOM ATOM	591 NZ LYS 592 C LYS	278	26.214	7.801	2.259	1.00 28.08
-0	ATOM	593 O LYS	278 278	23.862 23.866	7.317 6.091	8.361 8.271	1.00 25.78
50	ATOM	594 N ARG	279	24.388	7.950	9.400	1.00 26.96 1.00 26.39
	ATOM ATOM	595 CA ARG 596 CB ARG	279 279	24.999	7.195	10.482	1.00 27.59
	ATOM	597 CG ARG	279	26.266 27.190	7.893 8.219	10.953 9.794	1.00 28.22 1.00 31.75
55	ATOM	598 CD ARG	279	28.645	8.302	10.202	1.00 33.61
55	ATOM ATOM	599 NE ARG 600 CZ ARG	279 279	29.490 30.818	8.575	9.047	1.00 35.68
	ATOM	601 NH1 ARG	279	31.478	8.479 8.108	9.035 10.128	1.00 38.22 1.00 38.46
	MOTA	602 NH2 ARG	279	31.488	8.760	7.920	1.00 37.61
60	MOTA ATOM	603 C ARG 604 O ARG	279 279	24.053 24.397	6.936 6.217	11.652	1.00 27.34
	ATOM	605 N ILE	280	22.854	7.503	12.589 11.596	1.00 28.95 1.00 25.28
	ATOM ATOM	606 CA ILE	280	21.886	7.270	12.661	1.00 24.59
	ATOM	607 CB ILE 608 CG2 ILE	280 280	20.922 19.884	8.464 8.152	12.827	1.00 22.88
65	ATOM	609 CG1 ILE	280	21.708	9.722	13.912 13.219	1.00 21.69 1.00 21.57
	ATOM	610 CD1 ILE	280		10.965	13.380	1.00 20.98
	ATOM ATOM	611 C ILE	280 280	21.085 20.181	6.014	12.315	1.00 24.77
70	ATOM	613 N THR	281	21.421	6.051 4.902	11.481	1.00 23.84 1.00 25.98
70	ATOM ATOM	614 CA THR	281	20.754	3.628	12.706	1.00 27.40
	MOTA	615 CB THR 616 OG1 THR	281 281	21.064 22.485	2.608	13.805	1.00 28.22
	ATOM	617 CG2 THR	281	20.518	2.514 1.237	13.970 13.422	1.00 32.17 1.00 30.45
<i>7</i> 5	ATOM	618 C THR	281	19.236	3.720	12.547	1.00 26.89
75	ATOM ATOM	619 O THR 620 N GLY	281 282	18.685	3.173	11.596	1.00 27.85
	MOTA	621 CA GLY	282	18.568 17.120	4.405 4.536	13.468 13.395	1.00 25.97 1.00 24.93
	MOTA	622 C GLY	282	16.605	5.255	12.156	1.00 25.15
80	ATOM ATOM	623 O GLY 624 N PHE	282 283	15.502 17.400	4.981	11.680	1.00 23.70
- <b>-</b>	ATOM	625 CA PHE	283	17.400	6.187 6.948	11.639 10.439	1.00 24.97 1.00 25.33
	ATOM	626 CB PHE	283	17.958	8.169	10.295	1.00 23.33
_	ATOM ATOM	627 CG PHE 628 CD1 PHE	283 283	17.757 18 377	8.945	9.017	1.00 23.75
85	ATOM	629 CD2 PHE	283	18.377 16.940	8.548 10.069	7.837 8.994	1.00 23.86 1.00 22.16
	MOTA	630 CE1 PHE	283	18.185	9.261	6.654	1.00 23.03

	ATOM	631	CE2 P	HE 283	16.743	10.784	7.820	1.00 23.21
	ATOM	632		HE 283	17.367		6.648	1.00 20.80
	MOTA	633		HE 283	17.141	6.072	9.185	1.00 25.72
_	ATOM	634		HE 283	16.287	6.128	8.295	1.00 26.38
5	MOTA	635	N M	ET 284	18.194	5.265	9.115	1.00 26.64
	MOTA	636	CA M	ET 284	18.384	4.398	7.960	1.00 28.17
	MOTA	637	CB M	ET 284	19.825	3.887	7.916	1.00 29.11
	ATOM	638	CG M	ET 284	20.836	4.994	7.618	1.00 30.38
	MOTA	639	SD M	ET 284	20.370	6.064	6.205	1.00 33.12
10	MOTA	640	CE M	ET 284	20.937	5.078	4.772	1.00 34.35
	MOTA	641	C M	ET 284	17.395	3.235	7.917	1.00 29.78
	MOTA	642		ET 284	17.313	2.516	6.917	1.00 28.85
	MOTA	643		LU 285	16.629	3.068	8.991	1.00 31.01
	ATOM	644		LU 285	15.638	1.999	9.060	1.00 31.97
15	MOTA	645		LU 285	15.439	1.536	10.507	1.00 33.56
	ATOM	646		LU 285	16.658	0.814	11.078	1.00 37.02
	ATOM	647		LU 285	16.417	0.259	12.469	1.00 38.77
	ATOM	648	OE1 G		15.390	0.617	13.090	1.00 39.52
	ATOM	649		LU 285	17.265	-0.529	12.942	1.00 40.58
20	ATOM	650		LU 285	14.306	2.444	8.479	1.00 31.93
	ATOM	651		LU 285	13.430	1.619	8.211	1.00 32.23
	ATOM	652		EU 286	14.153	3.754	8.289	1.00 32.23
	ATOM	653		EU 286	12.935	4.315	7.715	1.00 30.76
	ATOM	654		EU 286	12.890	5.835	7.931	
25	ATOM	655		EU 286	13.009	6.367	9.364	1.00 29.72 1.00 29.96
	MOTA	656	CD1 L		12.937	7.884	9.339	1.00 29.96
	ATOM	657	CD2 L		11.890	5.805	10.235	1.00 28.70
	ATOM	658		EU 286	12.960	4.011	6.220	
	ATOM	659		EU 286	14.021	3.715	5.666	1.00 29.96
30	ATOM	660		YS 287	11.814	4.075		1.00 30.54
00	ATOM	661		YS 287	11.821	3.791	4.123	1.00 30.89 1.00 31.57
	ATOM	662		YS 287	10.400	3.677	3.555	
	ATOM	663		YS 287	9.395	5.168	3.569	1.00 32.51
	ATOM	664		YS 287	12.579	4.921	3.457	1.00 35.47
35	ATOM	665		YS 287	12.504	6.071	3.437	1.00 31.76
Ž,	ATOM	666		LN 288	13.327	4.591		1.00 30.50
	ATOM	667		LN 288	14.134	5.591	2.411 1.723	1.00 32.56
	ATOM	668		LN 288	14.818	4.960	0.519	1.00 32.18
	ATOM	669		LN 288	16.070	5.697	0.319	1.00 34.37
40	ATOM	670		LN 288	16.766	4.982	-1.045	1.00 37.44
	ATOM	671	OE1 GI		16.178	4.741	-2.095	1.00 38.80
	ATOM	672	NE2 GI		18.023	4.626	-0.832	
	ATOM	673		LN 288	13.304	6.800	1.305	1.00 41.12
	MOTA	674		LN 288	13.809	7.918	1.213	
45	ATOM	675	N AS		12.019	6.586	1.063	1.00 29.76
	ATOM	676		SN 289	11.180	7.701	0.685	1.00 29.60 1.00 30.09
	ATOM	677	CB AS		9.789	7.222	0.320	1.00 30.09 1.00 32.43
	ATOM	678		SN 289	8.831	8.363	0.186	1.00 32.43
	ATOM	679	OD1 AS		8.262	8.837	1.177	1.00 37.17
50	ATOM	. 680	ND2 AS		8.670	8.850	-1.038	1.00 37.46
	ATOM	681	C AS		11.065	8.737	1.803	1.00 28.55
	ATOM	682	O AS		11.120	9.954	1.561	1.00 28.23
	ATOM	683	N AS		10.880	8.253	3.027	1.00 27.44
	ATOM	684	CA AS		10.750	9.146	4.166	1.00 25.42
55	ATOM	685	CB AS		10.100	8.423	5.351	1.00 25.58
	ATOM	686	CG AS		8.593	8.245	5.159	1.00 25.63
•	ATOM	687	OD1 AS		8.033	8.887	4.247	1.00 25.74
	ATOM	688	OD2 AS		7.966	7.479	5.918	1.00 24.50
	MOTA	689	C AS		12.116	9.712	4.541	1.00 24.26
60	ATOM	690	0 AS		12.205	10.793	5.113	1.00 23.09
	ATOM	691	N GI		13.176	8.984	4.203	1.00 24.37
	ATOM	692	CA GI		14.525	9.453	4.482	1.00 23.42
	MOTA	693	CB GI		15.562	8.400	4.092	1.00 23.59
	MOTA	694	CG GI		15.608	7.164	4.965	1.00 22.66
65	MOTA	695	CD GI		16.639	6173	4.464	1.00 22.68
	ATOM	696	OE1 GI		17.532	6.527	3.694	1.00 24.72
	ATOM	697	NE2 GI		16.532	4.930	4.908	1.00 24.25
	ATOM	698	C GI		14.773	10.704	3.649	1.00 23.72
	ATOM	699	O GI		15.328	11.688	4.134	1.00 21.67
70	ATOM	700	N II		14.358	10.648	2.384	1.00 23.54
	ATOM	701	CA II		14.541	11.765	1.462	1.00 23.40
	ATOM	702	CB II		14.166	11.363	-0.003	1.00 24.40
	MOTA	703	CG2 II		14.176	12.592	-0.913	1.00 24.00
	ATOM	704	CG1 II		15.160	10.326	-0.535	1.00 25.84
<i>7</i> 5	ATOM	705	CD1 II		16.582	10.825	-0.554	1.00 28.34
	ATOM	706	CII		13.681	12.938	1.903	1.00 22.88
	ATOM	707	o ii		14.148	14.078	1.952	1.00 22.08
	ATOM	708	N L		12.430	12.649	2.245	1.00 22.08
	ATOM	709	CA LE		11.513	13.679	2.684	1.00 21.21
80	ATOM	710	CB LE		10.128	13.077	2.945	1.00 22.20
	MOTA	711	CG LI		9.337	12.783	1.668	1.00 26.65
	MOTA	712	CD1 Li		8.100	11.943	1.981	1.00 27.63
	MOTA	713	CD2 LE		8.947	14.115	1.009	1.00 27.83
_	MOTA	714	C L		12.041	14.366	3.936	1.00 27.30
<b>85</b> .	ATOM	715	O L		12.013	15.588	4.034	1.00 20.74
J	ATOM	716	N L		12.532	13.578	4.887	1.00 20.74
	ALON	, 10	44 11	234	12.33% A	23.373	4.00/	1.00 22.09
					•			

				33	
	ATOM	717 CA LEU	204	13 053 34 550 5 55	
	ATOM		294	13.053 14.158 6.111	
	ATOM		294	13.410 13.062 7.120	
			294	12.210 12.367 7.770	
5	ATOM	720 CD1 LEU	294	12.693 11.448 8.877	1.00 23.93
9	ATOM	721 CD2 LEU	294	11.254 13.400 8.339	
	MOTA	722 C LEU	294	14.262 15.034 5.818	
	MOTA	723 O LEU	294	14.371 16.138 6.335	
	MOTA	724 N LEU	295	15.170 14.549 4.979	
10	MOTA	725 CA LEU	295	16.352 15.334 4.636	
10	ATOM	726 CB LEU	295	17.325 14.481 3.836	
	ATOM	727 CG LEU	295	18.087 13.499 4.725	
	ATOM	728 CD1 LEU	295		
	ATOM	729 CD2 LEU	295		
	ATOM				
15			295	16.020 16.605 3.857	
10	ATOM	731 O LEU	295	16.537 17.682 4.158	1.00 19.82
	ATOM	732 N LYS	296	15.158 16.473 2.855	1.00 21.79
	ATOM	733 CA LYS	296	14.769 17.605 2.029	1.00 25.11
	MOTA	734 CB LYS	296	13.821 17.139 0.919	1.00 27.17
20	ATOM	735 CG LYS	296	13.241 18.257 0.084	1.00 30.32
20	ATOM	736 CD LYS	296	12.261 17.694 -0.938	
	MOTA	737 CE LYS	296	11.800 18.766 -1.903	1.00 33.40
	ATOM	738 NZ LYS	296		1.00 35.42
	ATOM	739 C LYS	296		1.00 37.44
	ATOM	740 O LYS	296		1.00 23.87
25	ATOM	741 N SER	297		1.00 23.29
	ATOM			13.287 18.326 3.798	1.00 23.52
	ATOM		297	12.587 19.294 4.628	1.00 24.66
		743 CB SER	297	11.243 18.707 5.086	1.00 25.85
	ATOM	744 OG SER	297	11.426 17.494 5.798	1.00 25.78
30	ATOM	745 C SER	297	13.374 19.791 5.852	1.00 24.58
30	MOTA	746 O SER	297	13.123 20.898 6.338	1.00 25.12
	ATOM	747 N GLY	298	14.333 19.002 6.328	1.00 22.15
	ATOM	748 CA GLY	298	15.068 19.406 7.511	
	ATOM	749 C GLY	298		1.00 22.02
	ATOM	750 O GLY	298		1.00 20.47
35	ATOM	751 N CYS	299		1.00 20.04
-	ATOM			17.203 19.363 6.306	1.00 20.94
			299	18.649 19.543 6.237	1.00 21.39
	MOTA	753 CB CYS	299	19.182 19.250 4.827	1.00 23.06
	ATOM	754 SG CYS	299	18.429 20.203 3.482	1.00 29.00
40	ATOM	755 C CYS	299	19.039 20.951 6.658	1.00 20.07
40	MOTA	756 O CYS	299	19.907 21.121 7.506	1.00 18.32
	ATOM .	757 N LEU	300	18.379 21.958 6.097	1.00 18.43
	ATOM	758 CA LEU	300	18.704 23.335 6.443	1.00 18.89
	ATOM	759 CB LEU	300	17.942 24.303 5.540	
	MOTA	760 CG LEU	300		1.00 17.66
45	ATOM	761 CD1 LEU	300		1.00 18.57
	ATOM	762 CD2 LEU	300		1.00 18.04
	ATOM	763 C LEU		17.670 26.535 4.469	1.00 18.71
	ATOM		300	18.424 23.657 7.913	1.00 18.49
			300	19.151 24.435 8.535	1.00 18.49
50	ATOM	765 N GLU	301	17.368 23.061 8.462	1.00 18.69
50	MOTA	766 CA GLU	301	17.020 23.278 9.858	1.00 18.42
	ATOM	767 CB GLU	301	15.680 22.604 10.181	1.00 18.90
	MOTA	768 CG GLU	301	14.505 23.235 9.443	1.00 21.00
	MOTA	769 CD GLU	301	13.163 22.710 9.897	1.00 22.11
EE	MOTA	770 OE1 GLU	301	13.145 21.861 10.809	1.00 22.99
<b>55</b> .	MOTA	771 OE2 GLU	301	12.128 23.156 9.342	
	ATOM	772 C GLU	301	18.137 22.729 10.744	1.00 23.74
	ATOM	773 O GLU	301	18.488 23.327 11.764	1.00 18.45
	ATOM	774 N VAL	302		1.00 17.98
	ATOM	775 CA VAL	302	**	1.00 18.55
60	ATOM	776 CB VAL	302	**	1.00 18.30
	ATOM	777 CG1 VAL		20.165 19.597 10.631	1.00 17.49
	ATOM		302	21.417 19.094 11.337	1.00 17.23
•		778 CG2 VAL	302	19.003 18.660 10.888	1.00 18.62
	MOTA	779 C VAL	302	21.037 21.913 10.991	1.00 18.44
65	MOTA	780 O VAL	302	21.762 22.142 11.959	1.00 18.67
65	ATOM	781 N VAL	303	21.274 22.413 9.782	1.00 17.76
	ATOM	782 CA VAL	303	22.406 23.296 9.546	1.00 17.41
	ATOM	783 CB VAL	303	22.461 23.762 8.074	
	ATOM	784 CG1 VAL	303		1.00 17.57
	ATOM	785 CG2 VAL	303		1.00 16.57
<i>7</i> 0	ATOM	786 C VAL	303		1.00 18.12
. •	ATOM			22.260 24.528 10.435	1.00 18.40
			303	23.219 24.985 11.051	1.00 18.46
	MOTA	788 N LEU	304	21.043 25.057 10.495	1.00 17.81
	MOTA	789 CA LEU	304	20.771 26.237 11.296	1.00 18.40
<i>7</i> 5	ATOM	790 CB LEU	304	19.310 26.664 11.145	1.00 18.67
13	ATOM	791 CG LEU	304	18.905 27.901 11.954	1.00 18.74
	ATOM	792 CD1 LEU	304	19.798 29.072 11.572	1.00 19.24
	ATOM	793 CD2 LEU	304		
	ATOM	794 C LEU	304		1.00 19.46
0.5	ATOM	795 O LEU	304		1.00 19.34
80	ATOM	796 N VAL	305		1.00 18.80
	ATOM			20.720 24.811 13.265	1.00 19.25
	ATOM		305	20.984 24.439 14.655	1.00 19.61
		798 CB VAL	305	20.342 23.072 15.031	1.00 20.39
	MOTA	799 CG1 VAL	305	20.877 22.596 16.381	1.00 18.01
85	ATOM	800 CG2 VAL	305	18.819 23.192 15.081	1.00 18.19
00	ATOM	801 C VAL	305	22.495 24.320 14.828	1.00 20.18
	MOTA	802 O VAL	305	23.059 24.849 15.779	1.00 20.30

	ATOM	803	N	ARG	306	23.142	23.628	13.896	1.00 19.99
	MOTA	804	CA	ARG	306	24.587	23.456	13.957	1.00 21.89
	ATOM	805	CB	ARG	306	25.063	22.541	12.836	1.00 21.78
_	MOTA	806	CG	ARG	306	24.838	21.076	13.112	1.00 19.29
5	ATOM	807	CD	ARG	306	25.401	20.245	11.990	
•	MOTA	808	NE	ARG	306	25.516	18.853		1.00 20.34
	ATOM	809	CZ	ARG		26.166	17.928	12.393	1.00 22.00
					306			11.702	1.00 22.25
	ATOM	810	NH1		306	26.760	18.247	10.558	1.00 20.55
10	ATOM	811	NH2	ARG	306	26.241	16.692	12.173	1.00 22.86
10	MOTA	812	С	ARG	306	25.373	24.763	13.908	1.00 22.45
	ATOM	813	0	ARG	306	26.474	24.840	14.445	1.00 22.73
	MOTA	814	N	MET	307	24.805	25.785	13.277	1.00 24.18
	MOTA	815	CA	MET	307	25.470	27.084	13.169	1.00 26.27
4-	MOTA	816	CB	MET	307	24.608	28.046	12.353	1.00 27.38
15	MOTA	817	CG	MET	307	25.231	29.412	12.170	1.00 28.81
	ATOM	818	SD	MET	307	24.099	30.460	11.288	1.00 30.68
	ATOM	819	CE	MET	307	23.147	31.073	12.604	1.00 27.74
	ATOM	820	C	MET	307	25.763	27.708	14.532	1.00 25.58
	ATOM	821	ŏ	MET	307	26.731	28.453	14.701	
20	ATOM	822	Ŋ	CYS	308	24.921	27.400		
	ATOM	823	CA	CYS	308	25.087		15.505	1.00 26.62
	ATOM	824		CYS			27.935	16.842	1.00 25.94
			CB		308	23.901	27.512	17.693	1.00 27.50
	MOTA	825	SG	CYS	308	22.349	27.999	16.879	1.00 32.50
25	ATOM	826	C	CYS	308	26.411	27.483	17.451	1.00 25.08
25	MOTA	827	0	CYS	308	26.951	28.139	18.337	1.00 26.40
	ATOM	828	N	ARG	309	26.932	26.367	16.958	1.00 24.15
	MOTA	829	CA	ARG	309	28.212	25.836	17.426	1.00 23.77
	ATOM	830	CB	ARG	309	28.514	24.490	16.763	1.00 22.37
20	MOTA	831	CG	ARG	309	27.526	23.377	17.070	1.00 23.29
30	ATOM	832	CD	ARG	309	27.900	22.123	16.296	1.00 22.66
	MOTA	833	NE	ARG	309	29.133	21.499	16.778	1.00 23.68
	ATOM	834	CZ	ARG	309	30.260	21.397	16.079	1.00 22.00
	ATOM	835		ARG	309	30.337	21.884	14.850	1.00 20.45
	ATOM	836	NH2	ARG	309	31.309	20.777	16.612	1.00 21.98
35	MOTA	837	C	ARG	309	29.337	26.792	17.043	1.00 23.79
	ATOM	838	ō	ARG	309	30.334	26.918	17.758	1.00 23.79
	ATOM	839	Ň	ALA	310	29.167	27.438	15.892	1.00 23.32
	MOTA	840	CA	ALA	310	30.167	28.354	15.344	1.00 22.67
	ATOM	841	CB	ALA	310	30.501	27.953	13.903	1.00 23.22
40	ATOM	842	c	ALA	310	29.690	29.796	15.376	
	ATOM	843	ŏ	ALA	310	29.895	30.549	14.424	1.00 22.59
	ATOM	844	Ŋ	PHE	311	29.047	30.170	16.471	1.00 22.73
	ATOM	845	CA	PHE	311	28.552	31.524	16.639	1.00 23.10
	ATOM	846	CB	PHE	311	27.025	31.516	16.677	1.00 22.61
45	ATOM	847	CG	PHE	311	26.419	32.879	16.811	1.00 24.45
	MOTA	848	CD1		311	26.166	33.422	18.066	
	ATOM	849	CD2		311	26.111	33.625	15.677	1.00 25.03
	ATOM	850	CE1		311	25.610	34.697	18.189	1.00 24.86 1.00 26.19
	ATOM	851	CE2		311	25.555	34.904	15.787	
50	ATOM	852	cz	PHE	311	25.303	35.440	17.044	1.00 25.65
	ATOM	853	Č	PHE	311	29.118	32.064	17.950	1.00 25.80
	ATOM	854	ŏ	PHE	311	29.225	31.332	18.926	1.00 23.95
	ATOM	855	Ŋ	ASN	312	29.496	33.336		1.00 24.13
	ATOM	856	CA	ASN	312	30.041		17.965	1.00 23.37
55	ATOM	857	CB	ASN			33.928	19.170	1.00 23.53
00	ATOM		CG		312	31.413	34.524	18.884	1.00 24.46
		858		ASN	312	32.066	35.059	20.125	1.00 25.90
	ATOM	859	OD1		312	31.439	35.112	21.187	1.00 28.29
	ATOM	860	ND2		312	33.326	35.465	20.009	1.00 25.97
60	ATOM	861		ASN	312	29.091	35.015	19.670	1.00 23.70
OO	ATOM	862		ASN	312	29.051	36.121	19.127	1.00 22.7,0
	ATOM	863	Ŋ	PRO	313	28.309	34.707	20.715	1.00 23.93
	MOTA	864	CD	PRO	313	28.291	33.413	21.415	1.00 24.49
	MOTA	865	CA	PRO	313	27.340	35.635	21.307	1.00 25.73
65	MOTA	866	CB	PRO	313	26.561	34.748	22.283	1.00 25.50
UJ	ATOM	867	CG	PRO	313	27.557	33.738	22.691	1.00 25.23
	ATOM	868	С	PRO	313	27.955	36.856	21.976	1.00 26.34
	MOTA	869	0	PRO	313	27.271	37.852	22.209	1.00 27.02
	MOTA	870		LEU	314	29.243	36.782	22.283	1.00 27.08
70	MOTA	871		LEU	314	29.933	37.908	22.900	1.00 28.42
70	MOTA	872		LEU	314	31.384	37.525	23.202	1.00 29.58
	ATOM	873		LEU	314	31.568	36.580	24.390	1.00 30.01
	MOTA	874	CD1		314	32.985	35.966	24.353	1.00 30.50
	MOTA	875	CD2		314	31.366	37.344	25.685	1.00 31.31
ワニ	ATOM	876		LEU	314	29.881	39.134	21.980	1.00 29.42
<i>7</i> 5	MOTA	877		LEU	314	29.618	40.247	22.438	1.00 29.09
	MOTA	878		ASN	315	30.119	38.918	20.685	1.00 28.55
	ATOM	879	CA	ASN	315	30.104	39.995	19.699	1.00 28.31
	MOTA	880		ASN	315	31.520	40.220	19.135	1.00 28.09
00	MOTA	881		ASN	315	32.114	38.966	18.488	1.00 28.61
80	MOTA	882	OD1		315	31.459	37.935	18.375	1.00 27.11
	ATOM	883	ND2		315	33.368	39.065	18.053	1.00 29.33
	MOTA	884		ASN	315	29.123	39.771	18.536	1.00 28.16
	MOTA	885		ASN	315	29.115	40.534	17.566	1.00 28.31
0=	ATOM	886		ASN	316	28.289	38.742	18.637	1.00 27.03
85	MOTA	887		ASN	316	27.322	38.430	17.582	1.00 26.93
	ATOM	888		ASN	316	26.246	39.522	17.467	1.00 27.40

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				33	
	MOTA	889 . CG ASN	316	25.247 39.491	18.621 1.00 29.23
	MOTA	890 OD1 ASN	316		19.079 1.00 29.19
	ATOM	891 ND2 ASN	316		19.081 1.00 29.80
5	ATOM ATOM	892 C ASN 893 O ASN	316 316		16.226 1.00 25.60
_	ATOM	894 N THR	317		15.264 1.00 25.51
	ATOM	895 CA THR	317		16.162
	ATOM	896 CB THR	317		14.970 1.00 24.58
10	ATOM	897 OG1 THR	317		16.029 1.00 25.19
10	ATOM	898 CG2 THR	317	31.255 38.924 1	L5.194 1.00 24.84
	ATOM ATOM	899 C THR 900 O THR	317		l4.648 1.00 22.99
	ATOM	900 O THR 901 N VAL	317 318		15.559 1.00 22.92
	ATOM	902 CA VAL	318		13.388 1.00 22.45
15	ATOM	903 CB VAL	318		13.004 1.00 22.06 12.281 1.00 21.83
	ATOM	904 CG1 VAL	318		1.017 1.00 21.77
	ATOM	905 CG2 VAL	318		1.950 1.00 23.58
	ATOM	906 C VAL	318		12.081 1.00 21.76
20	MOTA MOTA	907 O VAL 908 N LEU	318 319		1.366 1.00 21.99
	ATOM	909 CA LEU	319		2.122 1.00 21.37
	ATOM	910 CB LEU	319		1.278 1.00 22.24 1.767 1.00 22.86
	ATOM	911 CG LEU	319		.1.767
25	MOTA	912 CD1 LEU	319		0.928 1.00 25.19
25	ATOM	913 CD2 LEU	319	33.896 28.116 1	1.475 1.00 24.34
	ATOM ATOM	914 C LEU 915 O LEU	319	31.684 31.528	9.833 1.00 23.30
	MOTA	915 O LEU 916 N PHE	319 320	30.687 30.870 32.389 32.194	9.551 1.00 22.87
	ATOM	917 CA PHE	320	32.389 32.194 32.037 32.176	8.925 1.00 23.64 7.508 1.00 25.23
30	ATOM	918 CB PHE	320	31.108 33.346	7.508 1.00 25.23 7.172 1.00 24.27
	ATOM	919 CG PHE	320	30.699 33.397	5.729 1.00 25.29
	ATOM	920 CD1 PHE	320		5.229 1.00 25.59
	ATOM ATOM	921 CD2 PHE	320		4.865 1.00 24.72
35	ATOM	922 CE1 PHE 923 CE2 PHE	320		3.894 1.00 25.95
	ATOM	924 CZ PHE	320 320		3.525 1.00 25.91
	MOTA	925 C PHE	320		3.040 1.00 25.81 6.702 1.00 26.25
	MOTA	926 O PHE	320		6.787 1.00 26.22
40	ATOM	927 N GLU	321	33.621 31.255	5.929 1.00 28.45
410	ATOM ATOM	928 CA GLU	321		5.125 1.00 29.34
	ATOM	929 CB GLU 930 CG GLU	321		4.006 1.00 29.96
	ATOM	931 CD GLU	321 321		2.999 1.00 31.85
45	ATOM	932 OE1 GLU	321		1.774 1.00 32.92 1.724 1.00 35.63
45	MOTA	933 OE2 GLU	321		0.855 1.00 31.62
	ATOM	934 C GLU	321	36.114 31.357	5.953 1.00 29.82
	ATOM	935 O GLU	321		5.602 1.00 29.97
	ATOM ATOM	936 N GLY 937 CA GLY	322 322		7.067 1.00 29.47
50	ATOM	938 C GLY	322		7.880 1.00 28.49
	ATOM	939 O GLY	322		9.062 1.00 27.90 9.882 1.00 28.38
	ATOM	940 N LYS	323		9.160 1.00 26.69
	ATOM	941 CA LYS	323	36.979 33.591 1	0.280 1.00 26.84
55	ATOM ATOM	942 CB LYS 943 CG LYS	323		9.878 1.00 28.64
-	ATOM	943 CG LYS 944 CD LYS	323 323		9.329 1.00 31.90
	ATOM	945 CE LYS	323		8.935 1.00 34.33 8.325 1.00 36.36
	MOTA	946 NZ LYS	323		8.325 1.00 36.36 9.323 1.00 38.14
60	MOTA	947 C LYS	323	25 600 24 000 -	0.707 1.00 25.87
00	ATOM	948 O LYS	323		9.961 1.00 23.69
	MOTA MOTA	949 N TYR 950 CA TYR	324		1.899 1.00 25.68
	ATOM	951 CB TYR	324 324		2,378 1.00 25.45
	ATOM	952 CG TYR	324		3.903 1.00 26.32 4.474 1.00 26.94
65	MOTA	953 CD1 TYR	324		1.237 1.00 27.29
	ATOM	954 CE1 TYR	324		1.722 1.00 28.49
	ATOM	955 CD2 TYR	324	32.858 33.491 15	5.215 1.00 25.92
	ATOM ATOM	956 CE2 TYR	324		5.702 1.00 26.59
70	ATOM	957 CZ TYR 958 OH TYR	324 324		.451 1.00 27.01
. •	ATOM	959 C TYR	324		5.920 1.00 28.62
	ATOM	960 O TYR	324		L.863 1.00 25.14 L.781 1.00 25.62
	ATOM	961 N GLY	325		1.507 1.00 23.90
75	ATOM	962 CA GLY	325		.001 1.00 23.79
<i>7</i> 5	ATOM	963 C GLY	325	30.897 38.461 11	.441 1.00 25.33
	ATOM ATOM	964 O. GLY 965 N GLY	325		1.652 1.00 24.38
	ATOM	965 N GLY 966 CA GLY	326 326		.589 1.00 24.25
0.0	ATOM	967 C GLY	326		2.004 1.00 24.94 0.883 1.00 25.23
80	MOTA	968 O GLY	326		0.883 1.00 25.23 0.751 1.00 25.79
	ATOM	969 N MET	327		185 1.00 26.02
	MOTA	970 CA MET	327	25.953 40.401 10	1.190 1.00 27.32
	ATOM ATOM	971 CB MET	327		0.864 1.00 29.29
85	ATOM	972 CG MET 973 SD MET	327 327		416 1.00 32.37
	ATOM	974 CE MET	327		0.146 1.00 37.07 0.596 1.00 35.38

	ATOM	975 C M	ET 327	26.152	41.373	9.017	1.00 27.13
	MOTA		ET 327	25.592	41.172	7.950	1.00 25.51
	ATOM		LN 328	26.950	42.423	9.211	
_	MOTA		LN 328	27.198	43.392		1.00 27.79
5	ATOM	_	LN 328	28.025	44.571	8.138 8.662	1.00 29.04
_	MOTA		LN 328	29.460	44.204		1.00 31.55
	MOTA		LN 328	29.682	43.901	8.990	1.00 33.92
	MOTA	982 OE1 G				10.462	1.00 36.11
	ATOM	983 NE2 G		28.873	43.216	11.102	1.00 35.48
10				30.802	44.407	11.011	1.00 36.91
10	MOTA		LN 328	27.959	42.718	6.993	1.00 28.92
	MOTA		LN 328	27.970	43.193	5.864	1.00 28.52
	ATOM		ET 329	28.604	41.604	7.317	1.00 28.72
	ATOM		ET 329	29.368	40.813	6.366	1.00 27.66
15	MOTA		ET 329	29.998	39.633	7.124	1.00 29.67
15	MOTA		ET 329	30.698	38.584	6.294	1.00 30.31
	MOTA	990 SD M	ET 329	31.675	37.438	7.333	1.00 30.76
	MOTA	991 CE M	ET 329	30.395	36.763	8.395	1.00 27.38
	MOTA	992 C M	ET 329	28.462	40.322	5.228	1.00 27.08
	ATOM	993 O M	ET 329	28.927	40.093	4.115	1.00 25.67
20	MOTA		HE 330	27.166	40.197	5.505	1.00 25.56
	ATOM		HE 330	26.202	39.717		
	ATOM		HE 330	25.258		4.510	1.00 25.27
	ATOM		HB 330		38.717	5.164	1.00 26.21
	ATOM			25.960	37.546	5.779	1.00 26.31
25				26.573	36.591	4.979	1.00 26.75
20	MOTA	999 CD2 P		26.037	37.413	7.160	1.00 27.20
	ATOM	1000 CE1 P		27.263	35.514	5.547	1.00 28.46
	ATOM	1001 CE2 P		26.722	36.342	7.737	1.00 28.83
	MOTA	1002 CZ PI	HE 330	27.337	35.391	6.928	1.00 27.19
00	MOTA	1003 C P	HE 330	25.368	40.812	3.858	1.00 24.89
30	MOTA		IE 330	24.351	40.536	3.226	1.00 24.85
•	MOTA		YS 331	25.803	42.051	4.007	
	ATOM		rs 331	25.003			1.00 24.84
	ATOM		(S 331		43.181	3.452	1.00 25.68
	ATOM			25.923	44.442	3.602	1.00 27.69
35			/S 331	25.100	45.699	3.629	1.00 30.20
33	ATOM	1009 CD L		24.105	45.611	4.781	1.00 34.11
	ATOM	1010 CE L		23.238	46.853	4.879	1.00 35.87
	MOTA	1011 NZ L		22.167	46.684	5.903	1.00 37.65
	ATOM	1012 C L	/S 331	24.679	43.007	1.990	1.00 26.00
40	MOTA	1013 О Ц	'S 331	23.551	43.317	1.609	1.00 26.68
40	MOTA	1014 N A	A 332	25.594	42.493	1.182	1.00 26.27
	ATOM	1015 CA A	A 332	25.357	42.299	-0.242	1.00 26.94
	MOTA	1016 CB A		26.645	41.847	-0.917	
	MOTA	1017 C AI		24.211	41.348	-0.588	1.00 27.13
	ATOM	1018 O AI		23.687	41.398		1.00 27.68
45	ATOM	1019 N L				-1.705	1.00 28.00
	ATOM			23.817	40.492	0.356	1.00 26.04
	ATOM			22.709	39.566	0.119	1.00 25.55
		1021 CB LE		22.548	38.586	1.279	1.00 22.80
	MOTA	1022 CG LI		23.589	37.495	1.501	1.00 23.44
50	ATOM	1023 CD1 LE		23.127	36.616	2.659	1.00 21.98
50	ATOM	1024 CD2 LE		23.766	36.673	0.241	1.00 24.51
	MOTA	1025 C L		21.391	40.318	-0.048	1.00 25.80
	MOTA	1026 O LE	EU 333	20.454	39.807	-0.644	1.00 26.35
	ATOM	1027 N GI	Y 334	21.330	41.533	0.480	1.00 26.06
	ATOM	1028 CA GI	Y 334	20.115	42.307	0.387	1.00 27.61
55	MOTA	1029 C GI		18.980	41.627	1.127	
	ATOM	1030 O GI		17.821	41.762	0.743	1.00 28.38
	ATOM	1031 N SE		19.313			1.00 29.21
	ATOM	1032 CA SE		18.310	40.898	2.191	1.00 28.07
	ATOM				40.190	2.984	1.00 28.11
60	ATOM			18.251	38.723	2.551	1.00 29.24
00		1034 OG SE 1035 C SE		18.153	38.604	1.143	1.00 31.20
	ATOM			18.648	40.266	4.474	1.00 28.25
	ATOM	1036 O SE		18.816	39.235	5.134	1.00 27.31
	ATOM	1037 N AS		18.751	41.482	5.004	1.00 27.15
<b>6</b> E	ATOM	1038 CA AS		19.080	41.661	6.411	1.00 27.95
65	MOTA	1039 CB AS	P 336	19.182	43.146	6.758	1.00 28.40
	MOTA	1040 CG AS	P 336	20.462	43.776	6.256	1.00 31.17
	ATOM	1041 OD1 AS	P 336	21.300	43.061	5.671	1.00 30.76
	MOTA	1042 OD2 AS		20.630	45.000	6.450	1.00 33.65
	ATOM	1043 C AS		18.054	41.000		
70	ATOM	1044 O AS		18.393		7.321	1.00 27.32
	ATOM	1045 N AS			40.523	8.406	1.00 27.74
				16.799	40.985	6.887	1.00 26.73
	ATOM	1046 CA AS		15.748	40.364	7.678	1.00 27.00
	ATOM	1047 CB AS		14.383	40.532	6.982	1.00 29.56
<i>7</i> 5	ATOM	1048 CG AS		14.362	39.994	5.564	1.00 30.90
13	ATOM	1049 OD1 AS		15.434	39.888	4.931	1.00 32.90
	ATOM	1050 OD2 AS		13.251	39.693	5.066	1.00 32.99
	MOTA	1051 C AS	P 337	16.082	38.886	7.917	1.00 25.07
	ATOM	1052 O AS		15.948	38.375	9.031	1.00 23.90
0.0	ATOM	1053 N LE		16.537	38.210	6.873	1.00 23.72
80	ATOM	1054 CA LE		16.904	36.809		
	ATOM	1055 CB LE		17.174		6.997	1.00 23.15
	ATOM				36.212	5.618	1.00 21.77
		1056 CG LE		17.719	34.783	5.629	1.00 22.22
	ATOM	1057 CD1 LE		16.705	33.837	6.276	1.00 22.75
85	MOTA	1058 CD2 LE		18.021	34.355	4.206	1.00 20.63
U.J	ATOM	1059 C LE		18.144	36.668	7.880	1.00 22.07
	ATOM	1060 O LE	U 338	18.176	35.856	8.799	1.00 22.27
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	ATOM		VAL 339	19.165 37.47	7.610 1.00 22.77
	MOTA MOTA		VAL 339	20.388 37.40	8.403 1.00 23.12
_	MOTA		VAL 339 VAL 339	21.448 38.408 22.718 38.279	7.893 1.00 23.99
5	MOTA	1065 CG2	VAL 339	22.718 38.279 21.732 38.163	
	ATOM ATOM	1066 C	VAL 339	20.108 37.690	9.884 1.00 23.24
	ATOM	1067 O 1068 N	VAL 339 ASN 340	20.611 36.998 19.296 38.708	10.770 1.00 22.39
10	MOTA		ASN 340	19.296 38.708 18.973 39.065	
10	ATOM		ASN 340	18.205 40.391	
	MOTA MOTA	1071 CG 1072 OD1	ASN 340 ASN 340	19.134 41.592	11.610 1.00 30.44
	ATOM	1073 ND2		18.844 42.649 20.258 41.440	11.042 1.00 33.87
15	MOTA	1074 C	ASN 340	18.189 37.970	
15	ATOM ATOM		ASN 340	18.392 37.737	13.415 1.00 23.30
	ATOM		GLU 341 GLU 341	17.294 37.298 16.527 36.224	11.514 1.00 24.45
	ATOM		GLU 341	16.527 36.224 15.350 35.814	
20	ATOM		GLU 341	14.179 36.773	
20	ATOM ATOM	1080 CD (	GLU 341	12.945 36.239	10.681 1.00 34.84
	ATOM		GLU 341 GLU 341	12.720 35.013 12.187 37.038	10.750 1.00 37.24
	MOTA	1083 C (	GLU 341	17.432 35.027	10.096 1.00 37.28 12.417 1.00 23.12
25	MOTA MOTA		GLU 341	17.290 34.356	13.448 1.00 22.72
20	ATOM		ALA 342 ALA 342	18.365 34.766 19.304 33.664	11.506 1.00 21.14
	ATOM		ALA 342	19.304 33.664 20.158 33.498	11.684 1.00 20.58 10.442 1.00 19.08
	ATOM		ALA 342	20.193 33.943	10.442 1.00 19.08 12.906 1.00 21.25
30	MOTA MOTA		NLA 342 PHE 343	20.386 33.074	13.764 1.00 21.78
	ATOM		PHE 343	20.720 35.164 21.581 35.548	
	MOTA	1092 CB E	HE 343	22.201 36.933	14.105 1.00 23.79 13.864 1.00 22.95
	ATOM ATOM		PHE 343	23.487 36.906	13.083 1.00 22.10
35	ATOM	1094 CD1 F 1095 CD2 F		23.540 36.348 24.644 37.480	11.814 1.00 21.63
	MOTA	1096 CE1 F		24.644 37.480 24.724 36.366	13.607 1.00 22.10 11.079 1.00 22.66
	ATOM		HE 343	25.831 37.503	12.880 1.00 20.80
	MOTA MOTA		HE 343	25 871 36.945	11.614 1.00 21.73
40	ATOM		HE 343	20.820 35.563 21.348 35.143	15.437 1.00 24.28 16.466 1.00 25.24
	ATOM		SP 344	19.581 36.042	16.466 1.00 25.24 15.422 1.00 25.30
	ATOM ATOM		SP 344 SP 344	18.807 36.088	16.655 1.00 27.20
4	ATOM		SP 344 SP 344	17.453 36.754 17.581 38.215	16.425 1.00 30.33
45	ATOM	1105 OD1 A	SP 344	18.728 38.719	16.084 1.00 34.37 16.068 1.00 36.85
	ATOM ATOM	1106 OD2 A		16.529 38.853	15.835 1.00 36.92
	ATOM		SP 344 SP 344	18.600 34.674 18.728 34.400	17.165 1.00 25.45
EΩ	MOTA	1109 N . P		18.728 34.400 18.274 33.770	18.364 1.00 25.36 16.250 1.00 24.47
50	ATOM		HE 345	18.072 32.393	16.647 1.00 23.12
	ATOM ATOM		HE 345 HE 345	17.703 31.513	15.457 1.00 23.28
	ATOM	1113 CD1 P		17.733 30.058 16.777 29.512	15.784 1.00 22.38 16.633 1.00 22.93
55	ATOM	1114 CD2 P	HE 345	18.773 29.250	16.633 1.00 22.93 15.329 1.00 22.45
55	MOTA MOTA		HE 345	16.856 28.183	17.036 1.00 21.83
	ATOM		HE 345 HE 345	18.861 27.919 17.901 27.385	15.724 1.00 22.15
	MOTA	1118 C P	HE 345	19.333 31.825	16.582 1.00 23.05 17.281 1.00 22.93
60	ATOM ATOM		HE 345	19.286 31.241	18.360 1.00 22.27
00	ATOM		LA 346 LA 346	20.459 31.982 21.712 31.457	16.592 1.00 23.50
	ATOM		LA 346	21.712 31.457 22.839 31.734	17.099 1.00 25.20 16.127 1.00 26.42
	ATOM	1123 C A	LA 346	22.038 32.040	16.127 1.00 26.42 18.459 1.00 27.60
65	ATOM ATOM	1124 O AI 1125 N LI		22.459 31.314	19.349 1.00 25.96
00	ATOM	1125 N L		21.843 33.348 22.127 33.985	18.620 1.00 28.41
	ATOM	1127 CB LY		22.127 33.985 21.838 35.485	19.901 1.00 30.85 19.841 1.00 32.36
	ATOM	1128 CG LY		21.860 36.147	21.202 1.00 36.99
70	ATOM ATOM	1129 CD LY		21.431 37.613	21.140 1.00 39.60
. •	ATOM	1130 CE LY		21.227 38.185 22.459 38.130	22.561 1.00 42.60
	MOTA	1132 C LY		21.298 33.355	23.428 1.00 42.88 21.011 1.00 30.95
	ATOM	1133 O LY		21.847 32.949	22.039 1.00 31.24
75	ATOM ATOM	1134 N AS		19.986 33.259	20.807 1.00 30.97
. •	ATOM	1135 CA AS 1136 CB AS		19.121 32.676 17.645 32.804	21.826 1.00 32.18
	ATOM	1137 CG AS	N 348	17.173 34.246	21.435 1.00 34.34 21.450 1.00 38.72
	MOTA	1138 OD1 AS	N 348	17.656 35.057	22.247 1.00 40.24
80	ATOM ATOM	1139 ND2 AS 1140 C AS		16.222 34.579	20.574 1.00 39.22
	ATOM	1140 C AS		19.457 31.227 19.442 30.838	22.149 1.00 30.79
	MOTA	1142 N LE	U 349	19.776 30.425	23.316 1.00 30.95 21.138 1.00 29.90
	ATOM	1143 CA LE	U 349	20.122 29.033	21.409 1.00 29.04
85	ATOM ATOM	1144 CB LE 1145 CG LE		20.298 28.238 20.380 26.738	20.108 1.00 29.41
-	ATOM	1146 CD1 LE		20.380 26.738 19.012 26.269	20.388 1.00 28.84 20.904 1.00 29.78
					43.70

	ATOM	1147	CD2	LEU	349	20.756	25.976	19.136	1 00 20 10
	ATOM	1148	c	LEU					1.00 30.12
					349	21.419	28.977	22.212	1.00 28.27
	ATOM	1149	0	LEU	349	21.527	28.229	23.181	1.00 28.13
_	MOTA	1150	N	CYS	350	22.405	29.768	21.802	1.00 27.19
5	MOTA	1151	CA	CYS	350	23.689	29.804	22.498	1.00 27.50
_	MOTA	1152	CB	CYS	350	24.610			
							30.856	21.875	1.00 27.40
	MOTA	1153	SG	CYS	350	25.370	30.336	20.331	1.00 30.05
	MOTA	1154	С	CYS	350	23.530	30.112	23.979	1.00 27.44
_	ATOM	1155	0	CYS	350	24.280	29.596	24.806	1.00 25.65
10	MOTA	1156	N	SER	351	22.551	30.944	24.316	
									1.00 28.30
	MOTA	1157	CA	SER	351	22.341	31.321	25.716	1.00 29.76
	MOTA	1158	CB	SER	351	21.239	32.377	25.835	1.00 27.97
	MOTA	1159	OG	SER	351	19.972	31.819	25.545	1.00 27.29
	ATOM	1160	С	SER	351	21.998	30.143	26.618	
15	ATOM	1161	ŏ	SER					1.00 30.56
10					351	22.104	30.253	27.835	1.00 30.76
	ATOM	1162	N	LEU	352	21.582	29.027	26.030	1.00 30.81
	MOTA	1163	CA	LEU	352	21.232	27.848	26.815	1.00 30.42
	MOTA	1164	CB	LEU	352	20.275	26.948	26.035	1.00 31.12
	ATOM	1165	CG	LEU	352				
20						19.035	27.615	25.410	1.00 31.69
20	MOTA	1166		LEU	352	18.055	26.553	24.966	1.00 31.69
	MOTA	1167	CD2	LEU	352	18.377	28.538	26.411	1.00 33.44
	MOTA	1168	С	LEU	352	22.479	27.071	27.206	1.00 30.67
	MOTA	1169	Ó	LEU	352	22.429	26.195		
	MOTA							28.070	1.00 31.08
25		1170	N	GLN	353	23.600	27.389	26.565	1.00 30.60
25	MOTA	1171	CA	GLN	353	24.871	26.733	26.869	1.00 31.59
	MOTA	1172	CB	GLN	353	25.265	27.050	28.315	1.00 34.06
	MOTA	1173	CG	GLN	353	25.542	28.519	28.575	
	MOTA	1174							1.00 37.01
			CD	GLN	353	26.850	28.959	27.955	1.00 39.88
20	ATOM	1175		GLN	353	27.890	28.318	28.156	1.00 43.06
30	ATOM	1176	NE2	GLN	353	26.818	30.061	27.209	1.00 41.20
	ATOM	1177	С	GLN	353	24.865	25.220	26.661	1.00 30.89
	ATOM	1178	ō	GLN	353				
						25.382	24.469	27.486	1.00 30.05
	MOTA	1179	N	LEU	354	24.294	24.772	25.550	1.00 28.93
25	MOTA	1180	CA	LEU	354	24.229	23.349	25.268	1.00 27.99
35	MOTA	1181	CB	LEU	354	23.373	23.082	24.026	1.00 28.43
	MOTA	1182	CG	LEU	354	21.881	23.406		
				LEU				24.046	1.00 30.02
	ATOM	1183			354	21.316	23.088	22.659	1.00 30.63
	MOTA	1184		LEU	354	21.15€	22.608	25.114	1.00 29.61
4.0	ATOM	1185	С	LEU	354	25.604	22.736	25.039	1.00 27.41
<b>40</b>	MOTA	1186	0	LEU	354	26.540	23.415	24.604	
	ATOM	1187	N						1.00 27.14
				THR	355	25.711	21.452	25.359	1.00 25.55
	MOTA	1188	CA	THR	355	26.933	20.693	25.147	1.00 24.53
	ATOM	1189	CB	THR	355	27.121	19.573	26.199	1.00 24.00
	ATOM	1190	OG1	THR	355	26.116	18.564	26.015	1.00 23.40
45	ATOM	1191	CG2		355				
						27.017	20.136	27.603	1.00 24.13
	ATOM	1192	Ċ	THR	355	26.750	20.026	23.785	1.00 24.40
	ATOM	1193	0	THR	355	25.650	20.047	23.226	1.00 23.30
	MOTA	1194	N	GLU	356	27.816	19.427	23.263	1.00 22.46
_	MOTA	1195	CA	GLU	356	27.754	18.756		
50	MOTA	1196	CB					21.971	1.00 24.63
00				GLU	356	29.141	18.242	21.582	1.00 24.58
	ATOM	1197	CG	GLU	356	30.075	19.358	21.170	1.00 26.29
	ATOM	1198	CD	GLU	356	29.831	19.832	19.745	1.00 23.74
	ATOM	1199	OE1	GLU	356	30.390	19.223	18.820	1.00 26.81
	MOTA	1200		GLU	356	29.078			
55							20.806	19.548	1.00 25.33
00	ATOM	1201	C	GLU	356	26.752	17.610	21.942	1.00 24.03
	ATOM	1202	0	GLU	356	26.081	17.400	20.933	1.00 23.02
	ATOM	1203	N	GLU	357	26.657	16.865	23.042	1.00 25.24
	ATOM	1204	ĆA	GLU	357	25.721	15.746	23.122	1.00 25.24
	MOTA	1205	CB	GLU	357				
60						25.870	15.011	24.460	1.00 25.58
50	ATOM	1206	CG	GLU	357	27.261	14.435	24.698	1.00 28.22
	ATOM	1207	CD	GLU	357	27.358	13.628	25.991	ל'1.00 29.5
	ATOM	1208	OE1	GLU	357	26.600	13.913	26.936	1.00 28.40
	MOTA	1209		GLU	357	28.210	12.712	26.064	1.00 31.71
	ATOM	1210	Ċ	GLU	357				
65						24.288	16.244	22.979	1.00 24.57
03	ATOM	1211	0	GLU	357	23.472	15.633	22.296	1.00 24.04
	ATOM	1212	N	GLU	358	23.989	17.359	23.628	1.00 25.23
	ATOM	1213	CA	GLU	358	22.655	17.933	23.560	1.00 25.61
	ATOM	1214	CB	GLU	358	22.508			
							18.998	24.639	1.00 27.12
70	ATOM	1215	CG	GLU	358	22.943	18.437	25.982	1.00 29.78
70	ATOM	1216	CD	GLU	358	22.986	19.447	27.078	1.00 31.57
	ATOM	1217	OE1	GLU	358	23.395	20.605	26.822	1.00 32.27
	MOTA	1218	OE2	GLU	358	22.632	19.067		
	ATOM	1219						28.215	1.00 32.12
			C	GLU	358	22.371	18.491	22.169	1.00 24.96
76	ATOM '	1220	0	GLU	358	21.254	18.349	21.668	1.00 24.25
<i>7</i> 5	MOTA	1221	N	ILE	359	23.371	19.113	21.542	1.00 22.67
	MOTA	1222	CA	ILE	359	23.188	19.645	20.191	
									1.00 22.78
	ATOM	1223	CB	ILE	359	24.404	20.490	19.744	1.00 23.34
	MOTA	1224	CG2		359	24.344	20.740	18.236	1.00 22.93
00	MOTA	1225	CG1	ILE	359	24.430	21.803	20.538	1.00 25.31
80	ATOM	1226		ILE	359	25.711	22.603	20.401	1.00 27.90
-	ATOM	1227	c	ILE					
					359	23.000	18.481	19.215	1.00 21.51
	ATOM	1228	0	ILE	359	22.223	18.570	18.272	1.00 21.39
	MOTA	1229	N	ALA	360	23.725	17.393	19.455	1.00 20.70
•	ATOM	1230	CA	ALA	360	23.629	16.208	18.617	1.00 20.02
85									
55	ATOM	1231	CB	ALA	360	24.617	15.140	19.104	1.00 19,77
	MOTA	1232	С	ALA	360	22.198	15.675	18.688	1.00 19.38
	•								

						0,		
	ATOM	1233	O ALA	360	21.528	15 540	12	
	ATOM	1234	N LEU	361	21.736		17.665 19.903	
	ATOM	1235	CA LEU	361	20.388		20.117	
=	ATOM	1236	CB LEU	361	20.184		21.600	
5	ATOM	1237	CG LEU	361	21.138	13.452	22.105	
	MOTA	1238	CD1 LEU	361	20.951	13.265	23.592	1.00 23.19
	ATOM	1239	CD2 LEU	361	20.882	12.151	21.358	1.00 22.76
	ATOM	1240	C LEU	361	19.285	15.817	19.642	1.00 19.52
10	ATOM ATOM	1241	O LEU	361	18.374	15.402	18.933	1.00 18.57
10	ATOM	1242 1243	N PHE	362	19.356	17.085	20.030	1.00 19.75
	ATOM	1243	CA PHE CB PHE	362	18.335	18.030	19.595	1.00 20.87
	ATOM	1245	CB PHE CG PHE	362	18.559		20.212	1.00 19.97
	MOTA	1246	CD1 PHE	362	17.537	20.429	19.788	1.00 20.58
15	ATOM	1247	CD2 PHE	362 362	16.186	20.224	20.036	1.00 22.23
20	ATOM	1248	CE1 PHE	362	17.925	21.590	19.127	1.00 21.76
	ATOM	1249	CE2 PHE	362	15.240	21.156	19.634	1.00 21.84
	ATOM	1250	CZ PHE	362	16.984 15.640	22.528	18.724	1.00 23.51
	ATOM		C PHE	362	18.306	22.314 18.161	18.974	1.00 21.56
20	ATOM		O PHE	362	17.233	18.189	18.067	1.00 20.26
	ATOM		N SER	363	19.476	18.253	17.461	1.00 21.41
	ATOM		CA SER	363	19.521	18.371	17.445	1.00 19.81
	ATOM		CB SER	363	20.963	18.572	15.991 15.498	1.00 20.02
0.5	ATOM		OG SER	363	21.728	17.396	15.663	1.00 18.56
25	ATOM		C SER	363	18.906	17.121	15.353	1.00 20.81 1.00 20.59
	MOTA		O SER	363	18.231	17.217	14.325	1.00 20.39
	ATOM	1259	N SER	364	19.124	15.954	15.957	1.00 20.37
	MOTA	1260	CA SER	364	18.541	14.729	15.406	1.00 19.20
20	MOTA	1261	CB SER	364	19.108	13.474	16.099	1.00 20.81
30	ATOM		OG SER	364	18.644	13.335		1.00 21.39
	MOTA	1263	C SER	364	17.007	14.772	15.538	1.00 20.41
	MOTA		O SER	364	16.293	14.283	14.662	1.00 20.80
	MOTA		n ala	365	16.503	15.374	16.614	1.00 20.02
35	ATOM		CA ALA	365	15.053	15.484	16.813	1.00 20.02
33	MOTA		CB ALA	365	14.734	15.950	18.227	1.00 20.30
	ATOM		C ALA	365	14.450	16.455	15.794	1.00 21.11
	MOTA		O ALA	365	13.337	16.252	15.324	1.00 19.92
	MOTA		N VAL	366	15.189	17.509	15.458	1.00 20.57
40	ATOM		CA VAL	366	14.720	18.473	14.468	1.00 19.45
40	ATOM ATOM		CB VAL	366	15.684	19.677	14.360	1.00 19.15
	ATOM		CG1 VAL	366	15.369	20.502	13.106	1.00 19.19
	MOTA		CG2 VAL	366	15.567	20.542	15.618	1.00 20.02
	ATOM		C VAL	366	14.617	17.786	13.107	1.00 19.50
45	ATOM		N LEU	366 367	13.686	18.038	12.352	1.00 19.45
	ATOM		CA LEU	367	15.576 15.602	16.911	12.811	1.00 19.31
	ATOM		CB LEU	367	16.975	16.176	11.550	1.00 21.04
	ATOM		CG LEU	367	17.117	15.534 14.679	11.335	1.00 21.11
	ATOM		CD1 LEU	367	17.139	15.585	10.070	1.00 21.76
50	ATOM		CD2 LEU	367	18.395	13.868	8.841	1.00 24.04
	ATOM		C LEU	367	14.540	15.073	10.138 11.520	1.00 19.99
	ATOM	1284 (	D LEU	367	13.819	14.924	10.541	1.00 20.91 1.00 19.56
	ATOM	1285 N	ILE	368	14.472	14.297	12.596	1.00 19.56
EE	MOTA	1286 (	CA ILE	368	13.521	13.199	12.699	1.00 21.53
55	ATOM		CB ILE	368	14.047	12.095	13.649	1.00 22.94
	MOTA		CG2 ILE	368	13.171	10.867	13.550	1.00 22.23
	ATOM		CG1 ILE	368	15.499	11.735	13.308	1.00 24.46
	MOTA		CD1 ILE	368	15.719	11.309	11.896	1.00 27.21
60	ATOM	1291 (		368	12.183	13.722	13.231	1.00 22.51
00	ATOM	1292 (		368	11.830	13.501	14.393	1.00 21.63
	ATOM		SER	369	11.446	14.424	12.370	1.00 22.24
	ATOM		A SER	369	10.155	14.986	12.750	1.00 24.12
	ATOM		B SER	369	10.063	16.449	12.332	1.00 24.27
65	ATOM		G SER	369	8.745	16.929	12.528	1.00 26.59
00	ATOM	1297 (		369	9.011	14.221	12.107	1.00 25.22
	ATOM ATOM	1298 C		369	8.921	14.140	10.884	1.00 23.14
	ATOM	1299 N		370	8.117	13.646	12.929	1.00 27.45
	ATOM		D PRO	370	8.169	13.553	14.402	1.00 28.35
70	ATOM		A PRO	370	6.981	12.888	12.393	1.00 28.35
	ATOM		B PRO G PRO	370	6.488	12.105	13.607	1.00 28.25
	ATOM	1304 C		370	6.765	13.054	14.746	1.00 29.61
	ATOM	1305 0		370 370	5.906	13.791	11.812	1.00 29.35
	ATOM	1306 N			4.920	13.310	11.254	1.00 29.26
<i>7</i> 5	ATOM		ASP A ASP	371 371	6.107 5.151	15.096	11.944	1.00 29.51
	ATOM		B ASP	371	5.132	16.074	11.450	1.00 30.84
	ATOM		G ASP	371	4.616	17.296	12.377	1.00 32.99
	ATOM		D1 ASP	371	3.508	16.962 16.390	13.765	1.00 35.86
00	ATOM		D2 ASP	371	5.311	17.270	13.853 14.763	1.00 36.71
80	MOTA	1312 C		371	5.355	16.549	10.007	1.00 37.76
	MOTA	1313 0		371	4.515	17.276	9.484	1.00 29.75 1.00 30.14
	ATOM	1314 N		372	6.455	16.162	9.364	1.00 28.07
	ATOM	1315 C		372	6.694	16.597	7.988	1.00 26.59
OF.	MOTA	1316 C	B ARG	372	8.030	16.075	7.458	1.00 25.22
85	ATOM		G ARG	372	9.252	16.430	8.291	1.00 23.03
	ATOM	1318 C	D ARG	372	9.412	17.926	8.486	1.00 22.25
								· · · · · · · · · · · · · · · · · · ·

	ATOM	1319	NE	ARG	372	10	732	10 200	0 040		22 22
	ATOM	1320	CZ	ARG	372		160	18.209	9.049		21.70
	ATOM	1321						19.412	9.412		21.40
					372		374	20.472	9.278		19.74
5	ATOM	1322	NH2	ARG	372		378	19.547	9.915	1.00	19.59
3	ATOM	1323	.c	ARG	372		590	16.079	7.081	1.00	27.64
	ATOM	1324	0	ARG	372	5.	186	14.917	7.172	1.00	26.49
	MOTA	1325	N	ALA	373	5.	120	16.943	6.193		27.44
	MOTA	1326	CA	ALA	373	4.	074	16.563	5.259		27.38
	MOTA	1327	СB	ALA	373		603	17.789	4.508		28.35
10	MOTA	1328	Ċ	ALA	373		585	15.504	4.276		
	ATOM	1329	ō	ALA	373		770				26.33
								15.464	3.945		26.14
	ATOM	1330	N	TRP	374		681	14.637	3.830		26.51
	MOTA	1331	CA	TRP	374		987	13.582	2.856	1.00	25.94
15	MOTA	1332	CB	TRP	374		795	14.153	1.674	1.00	28.23
15	MOTA	1333	CG	TRP	374	4.	231	15.435	1.047	1.00	30.91
	MOTA	1334	CD2	TRP	374	3.	112	15.543	0.146	1.00	31.01
	ATOM	1335	CE2	TRP	374	2.	936	16.922	-0.144		31.51
	MOTA	1336	CE3	TRP	374	2.	240	14.614	-0.438		30.75
	MOTA	1337	CD1	TRP	374		676	16.718	1.252		31.80
20	MOTA	1338	NE1		374		903	17.614	0.541		
	ATOM	1339	CZ2		374		920	17.390			31.78
	ATOM	1340							-0.998		31.60
				TRP	374		223	15.082	-1.289		32.14
	MOTA	1341		TRP	374		075	16.458	-1.556		31.37
25	ATOM	1342		TRP	374		690	12.310	3.365	1.00	24.31
23	ATOM	1343		TRP	374		926	11.384	2.588	1.00	23.56
	MOTA	1344		LEU	375	5.	039	12.258	4.648	1.00	24.62
	MOTA	1345	CA	LEU	375	5.	698	11.070	5.185		24.04
	MOTA	1346	CB	LEU	375	6.	074	11.282	6.657		24.87
	MOTA	1347		LEU	375		256	12.194	7.022		24.99
30	MOTA	1348	CD1		375		422	12.210	8.542		25.00
	ATOM	1349	CD2		375		543	11.686			
	ATOM	1350		LEU	375			9.853	6.367		25.29
							769		5.065		23.50
	ATOM	1351		LEU	375		584	9.946	5.366		23.84
35	ATOM	1352		LEU	376		318	8.721	4.632	1.00	23.94
55	MOTA	1353		LEU	376		540	7.489	4.471	1.00	24.75
	ATOM	1354		LEU	376	5.	202	6.595	3.423	1.00	24.43
	MOTA	1355	CG	LEU	376	5.	268	7.172	2.001	1.00	26.18
	ATOM	1356	CD1	LEU	376	6.	160	6.296	1.124		27.91
4.0	ATOM	1357	CD2	LEU	376	3.	858	7.260	1.415		26.56
40	ATOM	1358		LEU	376		355	6.711	5.783		25.66
	MOTA	1359		LEU	376		317	6.079	6.002		24.55
	ATOM	1360		GLU	377		359	6.758			
	ATOM	1361		GLU	377				6.654		26.36
	ATOM						284	6.063	7.938		27.47
45		1362		GLU	377		261	4.878	7.947		29.08
40	ATOM	1363		GLU	377		959	3.840	6.875		30.40
	MOTA	1364		GLU	377		773	2.574	7.010	1.00	32.62
	ATOM	1365	OE1		. 377		981	2.578	6.704	1.00	33.66
	MOTA	1366	OE2	GLU	377	6.	197	1.556	7.428	1.00	33.92
<b>-</b> 0	ATOM	1367	C	GLU	377	5.	602	7.037	9.077		27.62
50	ATOM	1368	0	GLU	377	6.	619	6.902	9.762		27.21
	ATOM	1369	N	PRO	378	4.	728	8.035	9.295		27.83
	MOTA	1370		PRO	378		483	8.329	8.561		27.90
	ATOM	1371		PRO	378		951	9.020	10.358		28.17
	ATOM	1372		PRO	378		794	10.004	10.167		29.14
55	MOTA	1373		PRO	378		707				
00	MOTA	1374						9.143	9.564		28.27
				PRO	. 378		015	8.458	11.776		29.36
	ATOM	1375		PRO	378		655	9.050	12.649		28.11
	ATOM	1376		ARG	379		349	. 7.328	12.008	1.00	28.75
60	ATOM	1377		ARG	379		339	6.714	13.331	1.00	30.40
60	MOTA	1378		ARG	379	3.	327	5.551	13.366	1.00	32.82
	MOTA	1379	CG .	ARG	379	2.:	361	5.554	14.559	1.00	38.05
	MOTA	1380	CD .	ARG	379	3.0	009	5.102	15.888		42.49
	ATOM	1381	NE .	ARG	379	3.	379	6.216	16.779		45.57
	ATOM	1382	CZ .	ARG	379		867	6.071	18.014		47.28
65	ATOM	1383	NH1		379		062	4.858	18.530		48.40
	ATOM	1384	NH2		379		145	7.142	18.752		
	ATOM	1385		ARG	379						48.86
							741	6.199	13.652		29.02
	MOTA	1386		ARG	379		230	6.334	14.773		29.03
70	MOTA	1387		LYS	380		377	5.611	12.647		28.46
70	MOTA	1388		LYS	380		706	5.058	12.791	1.00	29.03
	ATOM	1389		LYS	380	8.	109	4.391	11.481	1.00	30.34
	MOTA	1390		LYS	380		086	3.254	11.621		33.47
	ATOM	1391	CD :	LYS	380	9.	080	2.353	10.379	1.00	34.27
	MOTA	1392		LYS	380		739	1.647	10.196		35.69
<i>7</i> 5	ATOM	1393		LYS	380		814	0.565	9.162		37.30
_	ATOM	1394		LYS	380		557	6.196	13.137		29.26
	ATOM	1395		LYS	380		528	6.049			
									13.999		30.09
	ATOM	1396		VAL	381		480	7.330	12.466		27.49
80	ATOM	1397		VAL	381		314	8.501	12.713		27.12
OU	ATOM	1398		VAL	381		054	9.617	11.663		26.02
	MOTA	1399	CG1		381		821	10.888	12.038	1.00	25.31
	ATOM	1400	CG2		381	9.4	494_	9.140	10.280	1.00	25.42
	ATOM	1401		VAL	381		014	9.047	14.104		27.48
~-	ATOM	1402		VAL	381	9.		9.478	14.830		26.45
85	ATOM	1403		GLN	382		743	9.014	14.475		28.11
	ATOM	1404		GLN	382		324	9.508	15.775		29.95
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	ATOM	1405 CB GLN	382	5.803	9.505	15.873	1.00 31.75
	ATOM		382	5.302	10.011		
	MOTA MOTA	1407 CD GLN 1408 OE1 GLN	382 382	3.886	10.501		1.00 38.98
5	MOTA	1409 NE2 GLN	382	2.978 3.677	9.761 11.765		1.00 40.59
	ATOM	1410 C GLN	382	7.907	8.707		1.00 40.58 1.00 29.66
	ATOM	1411 O GLN	382	8.323	9.278		1.00 28.76
,	ATOM ATOM	1412 N LYS 1413 CA LYS	383 383	7.922	7.385	16.776	1.00 29.16
10	ATOM	1414 CB LYS	383	8.454 8.303	6.491 5.027	17.799 17.369	1.00 29.20
	ATOM	1415 CG LYS	383	6.860	4.503	17.326	1.00 30.44 1.00 33.92
	ATOM	1416 CD LYS	383	6.810	3.149	16.627	1.00 37.33
	MOTA MOTA	1417 CE LYS 1418 NZ LYS	383	5.486	2.419	16.837	1.00 39.20
15	ATOM	1418 NZ LYS 1419 C LYS	383 383	5.439	1.665	18.135	1.00 40.75
	ATOM	1420 O LYS	383	9.928 10.370	6.785 6.781	18.055 19.202	1.00 28.39
	MOTA	1421 N LEU	384	10.692	7.019	16.990	1.00 28.89 1.00 26.11
	MOTA	1422 CA LEU	384	12.117	7.324	17.138	1.00 25.71
20	MOTA MOTA	1423 CB LEU 1424 CG LEU	384	12.829	7.235	15.778	1.00 23.95
	ATOM	1424 CG LEU 1425 CD1 LEU	.384 384	14.332 15.102	7.536	15.718	1.00 22.17
	ATOM	1426 CD2 LEU	384	14.833	6.661 7.285	16.719 14.299	1.00 24.02
	MOTA	1427 C LEU	384	12.330	8.711	17.760	1.00 21.00 1.00 25.43
25	ATOM	1428 O LEU	384	13.157	8.867	18.663	1.00 25.70
20	ATOM MOTA	1429 N GLN 1430 CA GLN	385	11.591	9.714	17.294	1.00 24.38
	ATOM	1430 CA GLN 1431 CB GLN	385 385	11.748	11.054	17.846	1.00 24.43
	MOTA	1432 CG GLN	385	10.819 11.260	12.072 13.503	17.167	1.00 24.78
20	MOTA	1433 CD GLN	385	10.221	14.561	17.459 17.136	1.00 22.10 1.00 23.15
30	ATOM	1434 OE1 GLN	385	10.528	15.569		1.00 24.07
	ATOM	1435 NE2 GLN	385	8.996	14.350	17.592	1.00 19.99
	ATOM ATOM	1436 C GLN 1437 O GLN	385	11.449	11.040	19.347	1.00 24.85
	ATOM	1438 N GLU	385 386	12.101 10.449	11.731	20.125	1.00 23.88
35	ATOM	1439 CA GLU	386	10.093	10.265 10.170	19.745 21.159	1.00 25.17
	MOTA	1440 CB GLU	386	8.902	9.237	21.355	1.00 27.06 1.00 30.30
	MOTA	1441 CG GLU	386	7.581	9.951	21.578	1.00 36.42
	ATOM ATOM	1442 CD GLU 1443 OE1 GLU	386	6.470	8.966	21.878	1.00 40.38
<b>4</b> 0	ATOM	1443 OE1 GLU 1444 OE2 GLU	386 386	5.997	8.309	20.923	1.00 42.90
	ATOM	1445 C GLU	386	6.094 11.271	8.828 9.661	23.068 21.978	1.00 43.27
	ATOM	1446 O GLU	386	11.563	10.198	23.044	1.00 25.28 1.00 25.32
	ATOM	1447 N LYS	387	11.932	8.619	21.476	1.00 23.32
45	ATOM ATOM	1448 CA LYS	387	13.088	8.038	22.148	1.00 24.19
10	ATOM	1449 CB LYS 1450 CG LYS	387 387	13.532	6.769	21.434	1.00 24.48
	MOTA	1451 CD LYS	387	12.526 12.849	5.645 4.512	21.544 20.605	1.00 25.85
	ATOM	1452 CE LYS	387	11.751	3.477	20.656	1.00 26.31 1.00 25.95
50	ATOM	1453 NZ LYS	387	11.950	2.448	19.620	1.00 27.79
50	ATOM ATOM	1454 C LYS 1455 O LYS	387	14.244	9.031	22.191	1.00 24.21
	ATOM	1455 O LYS 1456 N ILE	387 388	14.972 14.410	9.104	23.175	1.00 21.82
	ATOM	1457 CA ILE	388	15.465	9.783 10.786	21.109 21.033	1.00 23.57
55	ATOM	1458 CB ILE	388	15.484	11.463	19.637	1.00 23.44 1.00 21.69
33	ATOM	1459 CG2 ILE	388	16.394	12.678	19.646	1.00 22.46
	ATOM ATOM	1460 CG1 ILE 1461 CD1 ILE	388	15.936	10.449	18.588	1.00 23.21
	ATOM	1461 CD1 ILE 1462 C ILE	388 388	15.987	11.002	17.186	1.00 23.27
<b>~</b> 0	MOTA	1463 O ILE	388	15.234 16.145	11.840 12.173	22.113 22.872	1.00 22.84
60	MOTA	1464 N TYR	389	14.009	12.351	22.198	1.00 22.21 1.00 22.43
	ATOM	1465 CA TYR	389	13.695	13.363	23.197	1.00 24.16
	MOTA MOTA	1466 CB TYR 1467 CG TYR	389	12.268	13.868	23.003	1.00 25.05
	ATOM	1467 CG TYR 1468 CD1 TYR	389 389	12.164	14.996	22.000	1.00 26.11
65	ATOM	1469 CE1 TYR	389	11.103 10.971	15.057 16.124	21.093 20.203	1.00 26.57
	ATOM	1470 CD2 TYR	389	13.101	16.037	21.990	1.00 25.71 1.00 28.12
	ATOM	1471 CE2 TYR	389	12.975	17.115	21.102	1.00 27.45
	ATOM	1472 CZ TYR	389	11.906	17.149	20.215	1.00 26.96
70	ATOM ATOM	1473 OH TYR 1474 C TYR	389	11.754	18.218	19.356	1.00 28.94
	ATOM	1475 O TYR	389 389	13.876 14.337	12.802	24.607	1.00 24.83
	ATOM	1476 N PHE	390	13.514	13.502 11.537	25.503 24.794	1.00 24.78
	MOTA	1477 CA PHE	390		10.908	26.100	1.00 25.27 1.00 27.07
<i>7</i> 5	MOTA	1478 CB PHE	390	13.150	9.469	26.070	1.00 29.52
75	ATOM	1479 CG PHE	390	11.710	9.331	26.499	1.00 33.25
	ATOM ATOM	1480 CD1 PHE	390	10.839	8.482	25.807	1.00 34.80
	MOTA	1481 CD2 PHE 1482 CE1 PHE	390		10.029	27.609	1.00 34.21
00	ATOM	1483 CE2 PHE	390 390	9.499 9.895	8.325 9.882	26.208	1.00 35.97
80	ATOM	1484 CZ PHE	390	9.027	9.025	28.025 27.319	1.00 37.03 1.00 35.82
	ATOM	1485 C PHE	390	15.156	10.929	26.451	1.00 25.45
	ATOM	1486 O PHE	390	15.531	11.227	27.584	1.00 23.68
_	ATOM ATOM	1487 N ALA 1488 CA ALA	391 391		10.625		1.00 24.65
85	ATOM	1488 CA ALA 1489 CB ALA	391 391		10.627 10.116		1.00 24.20
-	ATOM	1490 C ALA	391		12.036		1.00 24.05
		_ <del>-</del>				,,	1.00 24.18

	MOTA	1491	.0	ALA	391	18.6	50	12.232	26.951	1.00 25.43
	MOTA	1492	N	LEU	392	17.4		13.014	25.201	1.00 24.17
	MOTA	1493	CA	LEU	392	17.8		14.402	25.410	1.00 23.73
	ATOM	1494	СВ	LEU	392	17.1		15.309	24.375	
5	ATOM	1495	CG	LEU	392	17.4		16.815		1.00 23.42
	MOTA	1496		LEU	392	18.9			24.510	1.00 21.24
	MOTA	1497		LEU				17.097	24.423	1.00 21.69
					392	16.6		17.571	23.423	1.00 22.29
	MOTA	1498	C	LEU	392	17.5		14.868	26.819	1.00 25.25
10	MOTA	1499	0	LEU	392	18.2		15.549	27.474	1.00 24.27
10	MOTA	1500	N	GLN	393	16.3	23	14.485	27.288	1.00 25.02
	MOTA	1501	CA	GLN	393	15.8	64	14.873	28.614	1.00 26.69
	ATOM	1502	CB	GLN	393	14.4		14.366	28.818	1.00 29.39
	ATOM	1503	CG	GLN	393	13.7		14.865	30.074	
	ATOM	1504	CD	GLN	393	12.2		14.569		1.00 34.04
15	ATOM	1505							30.079	1.00 36.82
10			OE1		393	11.8		13.411	29.996	1.00 37.30
	MOTA	1506	NE2		393	11.4		15.617	30.167	1.00 38.82
	MOTA	1507	С	GLN	393	16.7	83	14.349	29.724	1.00 26.46
	MOTA	1508	0	GLN	393	17.0	19	15.040	30.710	1.00 25.57
00	ATOM	1509	N	HIS	394	17.2	87	13.128	29.572	1.00 25.89
20	ATOM	1510	CA	HIS	394	18.19	90	12.559	30.569	1.00 26.72
	ATOM	1511	CB	HIS	394	18.3		11.049	30.375	1.00 27.82
	ATOM	1512	CG	HIS	394	17.0		10.289		
	ATOM	1513		HIS					30.776	1.00 31.60
					394	15.9		9.927	30.065	1.00 31.53
25	MOTA	1514		HIS	394	16.8		9.841	32.063	1.00 33.22
20	MOTA	1515		HIS	394	15.70		9.238	32.127	1.00 33.60
	MOTA	1516	NE2	HIS	394	15.14	46	9.276	30.929	1.00 34.06
	MOTA	1517	С	HIS	394	19.56	57	13.208	30.491	1.00 25.56
	MOTA	1518	0	HIS	394	20.1	55	13.552	31.513	1.00 25.72
	MOTA	1519	N	VAL	395	20.08		13.385	29.274	1.00 25.55
30	MOTA	1520	CA	VAL	395	21.40		13.993		
00	ATOM	1521	CB	VAL	395					1.00 24.89
						21.82		13.992	27.599	1.00 25.87
	MOTA	1522		VAL	395	23.09		14.815	27.399	1.00 25.30
	ATOM	1523		VAL	395	22.09		12.554	27.134	1.00 25.17
25	MOTA	1524	C	VAL	395	21.46		15.426	29.633	1.00 25.38
35	ATOM	1525	0	VAL	395	22.47	76	15.847	30.185	1.00 23.83
	MOTA	1526	N	ILE	396	20.36	56	16.162	29.488	1.00 24.76
	MOTA	1527	CA	ILE	396	20.31	LO	17.542	29.956	1.00 25.56
	ATOM	1528	CB	ILE	396	18.99		18.180	29.588	1.00 25.31
	ATOM	1529		ILE	396	18.72		19.465	30.382	
40	MOTA	1530		ILE	396	18.91		18.465		1.00 24.55
10	ATOM	1531		ILE					28.080	1.00 24.97
					396	17.55		18.989	27.593	1.00 24.29
	ATOM	1532	C	ILE	396	20.53		17.635	31.471	1.00 28.65
	ATOM	1533	0	ILE	396	21.13		18.583	31.960	1.00 28.05
45	ATOM	1534	N	GLN	397	20.04	16	16.639	32.203	1.00 31.32
<b>4</b> 5	ATOM	1535	CA	GLN	397	20.19	91	16.609	33.656	1.00 35.38
	MOTA	1536	CB	GLN	397	19.47	72	15.393	34.221	1.00 36.34
	MOTA	1537	CG	GLN	397	18.09		15.243	33.752	1.00 39.24
	ATOM	1538	CD	GLN	397	17.38		14.038	34.382	1.00 42.16
	ATOM	1539		GLN	397	17.99		12.971	34.522	
50	ATOM	1540		GLN	397	16.12		14.195		1.00 42.62
• •	ATOM	1541	C						34.755	1.00 43.91
	ATOM	1542		GLN	397	21.64		16.577	34.143	1.00 37.04
			0	GLN	397	21.93		17.049	35.240	1.00 37.11
	ATOM	1543	Ŋ	LYS	398	22.53		15.993	33.350	1.00 39.23
E E	MOTA	1544	CA	LYS	398	23.94		15.915	33.733	1.00 42.23
55	ATOM	1545	CB	LYS	398	24.74	12	15.089	32.720	1.00 40.46
	MOTA	1546	CG	LYS	398	24.19	3	13.689	32.476	1.00 39.92
	ATOM	1547	CD	LYS	398	25.17		12.833	31.675	1.00 39.62
	MOTA	1548	CE	LYS	398	25.43		13.434	30.286	1.00 39.22
	ATOM	1549	NZ	LYS	398	26.36		12.596	29.484	
60	ATOM	1550	c	LYS	398	24.55				1.00 37.98
00	ATOM	1551	ō	LYS	398			17.306	33.818	1.00 44.28
						25.54		17.535	34.529	1.00 44.44
	MOTA	1552	N	ASN	399	23.96		18.241	33.091	1.00 45.83
	MOTA	1553	CA	ASN	399	24.46		19.595	33.063	1.00 47.39
<b>/</b> E	ATOM	1554	CB	ASN	399	24.73		19.967	31.604	1.00 47.57
65	ATOM	1555	CG	ASN	399	25.34	8	18.807	30.803	1.00 47.79
	MOTA	1556	OD1	ASN	399	26.50		18.434	31.010	1.00 47.93
	MOTA	1557	ND2	ASN	399	24.56		18.226	29.896	1.00 48.24
	ATOM	1558	C	ASN	399	23.47		20.560		
	MOTA	1559	ŏ	ASN	399				33.710	1.00 49.01
70	ATOM					23.43		20.717	34.937	1.00 49.34
, 0		1560	N	HIS	400	22.67		21.186	32.861	1.00 50.43
	MOTA	1561	CA	HIS	400	21.65		22.160	33.240	1.00 52.29
	ATOM	1562	CB	HIS	400	20.73		22.349	32.046	1.00 51.08
	ATOM	1563	CG	HIS	400	21.47	5	22.344	30.750	1.00 50.35
75	ATOM	1564	CD2	HIS	400	21.65		21.368	29.832	1.00 50.24
<i>7</i> 5	ATOM	1565		HIS	400	22.21		23.419	30.316	1.00 50.79
	MOTA	1566		HIS	400	22.82		23.102		
	ATOM	1567							29.183	1.00 50.91
				HIS	400	22.49		21.862	28.871	1.00 49.91
	ATOM	1568	č	HIS	400	20.83		21.782	34.467	1.00 54.62
80	ATOM	1569	0	HIS	400	19.88		21.006	34.369	1.00 54.65
OU	MOTA	1570	N	LEU	401	21.21		22.343	35.618	1.00 56.91
	MOTA	1571	CA	LEU	401	20.48	7	22.061	36.854	1.00 59.10
	MOTA	1572	CB	LEU	401	21.30		22.469	38.081	1.00 59.50
	ATOM	1573	CG	LEU	401	21.08		21.490	39.244	1.00 60.29
	ATOM	1574		LEU	401	19.67		21.626	39.794	1.00 60.01
85		1575.								
55	MOTA			LEU/	401	21.31		20.062	38.748	1.00 59.79
	MOTA	1576	С	LEU	401	19.22	4	22.890	36.729	1.00 60.18

							40		
	MOTA	1577		LEU	401	19.275	24.017	36.220	1.00 61.06
	MOTA MOTA	1578 1579		ASP	402	18.097		37.188	1.00 60.81
	ATOM	1580		ASP ASP	402 402	16.814 16.766		37.016	1.00 61.03
5	ATOM	1581		ASP	402	16.409		37.711 39.205	1.00 62.09 1.00 63.42
	ATOM	1582		ASP	402	16.940		39.883	1.00 63.42
	ATOM	1583			402	15.609		39.716	1.00 63.96
	ATOM ATOM	1584 1585		ASP ASP	402 402	16.836	23.099	35.499	1.00 60.63
10	ATOM	1586		ASP	403	17.621 16.035	22.375 23.950	34.864 34.882	1.00 61.17
	MOTA	1587		ASP	403	16.083	23.943	33.430	1.00 59.71 1.00 57.97
	ATOM	1588		ASP	403	15.969	22.502	32.944	1.00 57.91
	MOTA ATOM	1589 1590		ASP ASP	403	14.749	21.799	33.538	1.00 58.27
15	ATOM	1591		ASP	403 403	13.789 14.74 <i>2</i>	21.500 21.570	32.785 34.774	1.00 57.61
	MOTA	1592		ASP	403	15.025	24.719	32.703	1.00 57.74 1.00 56.47
	ATOM	1593		ASP	403	15.042	25.947	32.631	1.00 56.67
	ATOM ATOM	1594 1595		GLU	404	14.097	23.936	32.157	1.00 54.01
20	ATOM	1596	CB	GLU	404 404	13.021 12.788	24.422 25.917	31.319	1.00 50.92
	ATOM	1597	CG	GLU	404	11.500	25.492	31.554 30.994	1.00 52.53 1.00 55.75
	ATOM	1598	CD	GLU	404	11.230	27.889	31.537	1.00 57.67
	ATOM	1599	OE1		404	10.211	28.503	31.134	1.00 58.54
25	ATOM ATOM	1600 1601	OE2	GLU GLU	404 404	12.041 13.714	28.371	32.375	1.00 58.20
	ATOM	1602	ŏ	GLU	404	13.121	24.171 24.300	29.977 28.907	1.00 47.15 1.00 46.59
	ATOM	1603	И	THR	405	14.986	23.774	30.070	1.00 43.07
	ATOM	1604	CA	THR	405	15.815	23.492	28.895	1.00 38.65
30	ATOM ATOM	1605 1606	CB OG1	THR THR	405 405	17.122	22.739	29.288	1.00 38.43
	ATOM	1607	CG2	THR	405 405	17.950 17.915	23.598 22.330	30.083 28.036	1.00 36.75
	ATOM	1608	C	THR	405	15.101	22.712	27.791	1.00 37.77 1.00 35.86
	ATOM	1609	0	THR	405	14.859	23.258	26.721	1.00 33.56
35	ATOM ATOM	1610 1611	N CA	LEU	406	14.749	21.449	28.039	1.00 34.04
	ATOM	1612	CB	LEU	406 406	14.083 13.653	20.668 19.290	27.000 27.516	1.00 32.51
	ATOM	1613	CG	LEU	406	13.758	18.137	26.500	1.00 32.98 1.00 31.34
	MOTA	1614		LEU	406	12.660	17.122	26.773	1.00 32.45
40	ATOM ATOM	1615 1616	CD2	LEU	406 406	13.645	18.644	25.077	1.00 32.35
-0	ATOM	1617	ŏ	LEU	406	12.856 12.625	21.395 21.414	26.456 25.253	1.00.31.91
	MOTA	1618	N	ALA	407	12.070	21.988	27.348	1.00 30.54 1.00 32.12
	ATOM	1619	CA	ALA	407	10.879	22.720	26.931	1.00 31.85
45	ATOM ATOM	1620 1621	CB C	ALA ALA	407 407	10.078	23.150	28.146	1.00 31.21
	ATOM	1622	ŏ	ALA	407	11.246 10.584	23.942 24.221	26.084 25.093	1.00 31.46
	ATOM	1623	N	LYS	408	12.296	24.667	26.473	1.00 31.62
	ATOM	1624	CA	LYS	408	12.723	25.849	25.718	1.00 30.77
50	MOTA MOTA	1625 1626	CB CG	LYS LYS	408 408	13.794 13.279	26.635	26.481	1.00 33.47
	MOTA	1627	CD	LYS	408	14.332	27.310 28.218	27.747 28.353	1.00 35.82 1.00 36.77
	ATOM	1628	CE	LYS	408	13.747	29.011	29.522	1.00 38.42
	ATOM ATOM	1629 1630	NZ	LYS	408	14.719	29.999	30.088	1.00 39.51
55	MOTA	1631	С 0	LYS LYS	408 408	13.263 13.158	25.462 26.229	24.351	1.00 28.18
	MOTA	1632	N	LEU	409	13.858	24.276	23.396 24.265	1.00 27.16 1.00 27.09
	ATOM	1633	CA	LEU	409	14.387	23.793	22.994	1.00 26.20
	ATOM ATOM	1634 1635	CB	LEU	409	15.246	22.546	23.210	1.00 24.61
60	MOTA	1636	CG CD1	LEU	409 409	16.608 17.347	22.793 21.465	23.844	1.00 25.33
	MOTA	1637	CD2		409	17.399	23.757	24.018 22.957	1.00 23.27
	ATOM	1638	C	LEU	409	13.228	23.462	22.057	1.00 26.11
	ATOM ATOM	1639 1640	O N	LEU	409	13.184	23.928	20.916	1.00 25.38
65	ATOM	1641	CA	ILE ILE	410 410	12.289 11.130	22.657 22.263	22.548	1.00 25.80
	ATOM	1642	CB	ILE	410	10.212	21.309	21.750 22.556	1.00 27.11 1.00 27.55
	ATOM	1643	CG2		410	8.831	21.225	21.915	1.00 29.14
	ATOM ATOM	1644	CG1		410	10.862	19.925	22.640	1.00 28.88
70	ATOM	1645 1646	CD1 C	ILE	410 410	10.227 10.324	18.999 23.477	23.672	1.00 29.04
	ATOM	1647	0	ILE	410	9.801	23.477	21.271 20.157	1.00 26.54 1.00 27.28
	ATOM	1648		ALA	411	10.240	24.504	22.108	1.00 26.52
	MOTA MOTA	1649		ALA	411	9.501	25.716	21.762	1.00 27.27
<i>7</i> 5	ATOM	1650 1651		ALA ALA	411 411	9.388	26.618	22.982	1.00 28.31
. •	ATOM	1652		ALA	411	10.187 9.600	26.473 27.379	20.618	1.00 28.07
	MOTA	1653	N	LYS	412	11.426	26.095	20.026	1.00 27.10 1.00 27.07
	ATOM	1654	CA	LYS	412	12.175	26.751	19.244	1.00 28.19
80	ATOM ATOM	1655 1656		LYS	412	13.680	26.756	19.579	1.00 28.62
-5	ATOM	1657		LYS LYS	412 412	14.067 15.559	27.694 27.615	20.728	1.00 30.34
	ATOM	1658		LYS	412	15.950	28.514	21.042 22.215	1.00 31.67 1.00 33.03
	ATOM	1659		LYS	412	15.797	29.985	21.964	1.00 35.05
85	ATOM ATOM	1660 1661		LYS LYS	412	11.955	26.117	17.864	1.00 27.51
	ATOM	1662		ILE	412 413	12.316 11.363	26.708 24.926	16.847 17.834	1.00 27.32 1.00 26.06
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	ATOM	1663	CA	ILE	413	11.105	24.202	16.588	1.00 26.80
	ATOM	1664	CB	ILE	413				
	ATOM					10.220	22.939	16.841	1.00 27.43
		1665		ILE	413	9.881	22.247	15.523	1.00 27.29
5	ATOM	1666		ILE	413	10.945	21.958	17.770	1.00 28.37
5	MOTA	1667	CD1	ILE	413	12.121	21.254	17.148	1.00 29.37
	ATOM	1668	С	ILE	413	10.433	25.057	15.519	1.00 26.56
	MOTA	1669	0	ILE	413	10.864	25.076	14.372	1.00 26.28
	ATOM	1670	N	PRO	414	9.359	25.775	15.882	1.00 27.37
	ATOM	1671	CD	PRO	414	8.700	25.857	17.198	1.00 26.88
10	ATOM	1672	CA	PRO	414	8.669	26.614		
10	ATOM	1673						14.897	1.00 26.65
			CB	PRO	414	7.427	27.080	15.658	1.00 27.87
	ATOM	1674	CG	PRO	414	7.903	27.129	17.070	1.00 29.01
	ATOM	1675	C	PRO	414	9.525	27.771	14.374	1.00 25.68
4 -	ATOM	1676	0	PRO	414	9.448	28.126	13.201	1.00 27.18
15	MOTA	1677	N	THR	415	10.352	28.342	15.241	1.00 25.08
	MOTA	1678	CA	THR	415	11.226	29.448	14.850	1.00 25.70
	MOTA	1679	CB	THR	415	11.944	30.028	16.089	1.00 27.08
	ATOM	1680		THR	415	10.964	30.406	17.060	1.00 27.92
	ATOM	1681		THR	415	12.768	31.250	15.727	
20									1.00 26.93
20	ATOM	1682	C	THR	415	12.260	28.954	13.825	1.00 23.76
	ATOM	1683	0	THR	415	12.546	29.624	12.839	1.00 23.92
	ATOM	1684	N	ILE	416	12.801	27.768	14.072	1.00 22.76
	ATOM	1685	CA	ILE	416	13.780	27.158	13.184	1.00 21.78
05	ATOM	1686	CB	ILE	416	14.175	25.760	13.711	1.00 22.29
25	ATOM	1687	CG2	ILE	416	14.921	24.976	12.648	1.00 21.98
	ATOM	1688	CG1	ILE	416	15.012	25.918	14.979	1.00 20.99
	ATOM	1689		ILE	416	15.190	24.634	15.776	1.00 22.24
	ATOM	1690	C	ILE	416	13.187	27.041		
								11.785	1.00 20.31
30	ATOM	1691	0	ILE	416	13.790	27.454	10.797	1.00 19.18
50	MOTA	1692	N	THR	417	11.988	26.480	11.710	1.00 20.67
	ATOM	1693	CA	THR	417	11.328	26.317	10.432	1.00 20.39
	ATOM	1694	CB	THR	417	10.048	25.508	10.602	1.00 21.40
	ATOM	1695	OG1	THR	417	10.390	24.228	11.147	1.00 20.70
~ =	ATOM	1696	CG2	THR	417	9.351	25.313	9.257	1.00 19.07
35	ATOM	1697	С	THR	417	11.026	27.661	9.785	1.00 20.61
	ATOM	1698	ō	THR	417	11.118	27.795	8.570	1.00 20.81
	ATOM	1699	Ň	ALA	418	10.674	28.651		
								10.605	1.00 21.09
	MOTA	1700	CA	ALA	418	10.367	29.987	10.118	1.00 20.90
40	ATOM	1701	CB	ALA	418	9.956	30.880	11.273	1.00 21.36
40	MOTA	1702	C	ALA	418	11.573	30.592	9.404	1.00 21.24
	ATOM	1703	0	ALA	418	11.441	31.157	8.321	1.00 19.90
	ATOM	1704	N	VAL	419	12.747	30.457	10.015	1.00 21.50
	ATOM	1705	CA	VAL	419	13.975	30.995	9.440	1.00 21.76
	ATOM	1706	CB	VAL	419	15.170	30.797	10.406	1.00 20.86
45	ATOM	1707	CG1		419	16.491	31.146	9.713	1.00 22.17
	ATOM	1708		VAL	419	14.969	31.655	11.648	
	MOTA	1709	C	VAL	419	14.282			1.00 23.28
	ATOM						30.328	8.104	1.00 21.71
		1710	0	VAL	419	14.586	30.997	7.120	1.00 21.28
50	ATOM	1711	N	CYS	420	14.180	29.006	8.065	1.00 20.93
50	ATOM	1712	CA	CYS	420	14.467	28.282	6.840	1.00 22.24
	MOTA	1713	СВ	CYS	420	14.560	26.782	7.137	1.00 20.03
	MOTA	1714	SG	CYS	420	15.994	26.393	8.177	1.00 21.62
	MOTA	1715	С	CYS	420	13.462	28.573	5.724	1.00 22.17
	ATOM	1716	0	CYS	420	13.815	28.560	4.545	1.00 22.39
55	ATOM	1717	N	ASN	421	12.213	28.843	6.090	1.00 22.88
	ATOM	1718	CA	ASN	421	11.213	29.165	5.083	1.00 23.16
	ATOM	1719	CB	ASN	421	9.803	29.189	5.686	
	ATOM	1720	CG	ASN	421	9.254	27.797		1.00 24.82
								5.945	1.00 26.54
60	ATOM	1721		ASN	421	9.691	26.821	5.332	1.00 28.43
00	ATOM	1722	ND2		421	8.274	27.703	6.841	1.00 28.17
	ATOM	1723	Ç	ASN	421	11.548	30.539	4.507	1.00 22.83 <sup>!</sup>
	ATOM	1724	0	ASN	421	11.372	30.783	3.311	1.00 23.42
	ATOM	1725	И	LEU	422	12.026	31.438	5.362	1.00 21.51
<b>-</b>	ATOM	1726	CA	LEU	422	12.394	32.773	4.912	1.00 21.12
65	ATOM	1727	CB	LEU	422	12.814	33.657	6.094	1.00 20.93
	ATOM	1728	CG	LEU	422	13.106	35.117	5.724	1.00 22.12
	ATOM	1729	CD1		422	11.914	35.708	4.998	1.00 23.58
	MOTA	1730		LEU	422	13.420	35.919		
								6.968	1.00 21.92
70	ATOM	1731	C	LEU	422	13.539	32.651	3.909	1.00 20.79
70	ATOM	1732	0	LEU	422	13.589	33.385	2.924	1.00 20.16
	MOTA	1733	N	HIS	423	14.457	31.721	4.162	1.00 20.32
	MOTA	1734	CA	HIS	423	15.569	31.496	3.246	1.00 19.09
	ATOM	1735	CB	HIS	423	16.480	30.377	3.774	1.00 19.51
	MOTA	1736	CG	HIS	423	17.357	29.757	2.726	1.00 20.42
<i>7</i> 5	ATOM	1737	CD2		423	18.560	30.132	2.233	1.00 22.15
	ATOM	1738	ND1		423	17.002	28.617	2.037	1.00 19.93
	ATOM	1739	CEI		423	17.945	28:317		
								1.164	1.00 21.28
	ATOM	1740	NE2		423	18.903	29.221	1.261	1.00 23.18
80	ATOM	1741	C	HIS	423	14.991	31.114	1.887	1.00 20.06
OU		. 1742	0	HIS	423	15.406	31.633	0.854	1.00 19.48
	MOTA	1743	N	GLY	424	14.025	30.202	1.897	1.00 20.89
	MOTA	1744	CA	GLY	424	13.409	29.779	0.656	1.00 21.77
	MOTA	1745	С	GLY	424	12.747	30.948	-0.045	1.00 22.46
	ATOM	1746	ō	GLY	424	12.854	31.092	-1.260	1.00 22.28
85	ATOM	1747	N	GLU	425	12.055	31.781	0.723	1.00 23.68
	ATOM	1748	CA	GLU	425	11.388	32.944	0.156	1.00 26.30
	,,,,,,,,,			ماحت					20.30

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	MOTA	1749		425	10.654 33.714 1.254 1.00 29.71
	MOTA MOTA	1750		425	9.438 32.987 1.807 1.00 34.81
_	ATOM	1751 1752		425 425	8.840 33.708 3.000 1.00 39.53 8.732 34.960 2.940 1.00 40.10
5	ATOM	1753		425	8.732 34.960 2.940 1.00 40.10 8.471 33.026 3.992 1.00 42.79
	ATOM	1754		425	12.380 33.862 -0.553 1.00 25.74
	ATOM ATOM	1755 1756		425	12.166 34.228 -1.708 1.00 26.36
	ATOM	1757		426 426	13.468 34.221 0.125 1.00 25.26 14.484 35.094 -0.470 1.00 25.80
10	ATOM .			426	14.484 35.094 -0.470 1.00 25.80 15.610 35.376 0.531 1.00 25.12
	MOTA	1759		426	15.150 36.115 1.775 1.00 28.49
	ATOM ATOM	1760 1761		426	14.489 37.445 1.415 1.00 29.27
	ATOM	1762		426 426	13.995 38.148 2.666 1.00 32.12 13.235 39.411 2.390 1.00 31 15
15	ATOM	1763		426	13.235 39.411 2.390 1.00 31.15 15.083 34.497 -1.733 1.00 25.06
	MOTA	1764	O LYS	426	15.363 35.209 -2.703 1.00 24.27
	ATOM	1765		427	15.278 33.183 -1.717 1.00 25.20
	ATOM ATOM	1766 1767		427	15.848 32.480 -2.857 1.00 26.06
20	ATOM	1768		427 427	16.165 31.032 -2.473 1.00 25.95 16.582 30.058 -3.581 1.00 27.66
	MOTA	1769		427	16.582 30.058 -3.581 1.00 27.66 17.718 30.638 -4.415 1.00 26.38
	ATOM	1770		427	17.002 28.740 -2.940 1.00 27.07
	MOTA MOTA	1771		427	14.922 32.523 -4.072 1.00 26.54
25	ATOM	1772 1773	O LEU N GLN	427 428	15.383 32.716 -5.194 1.00 26.46 13.622 32.369 -3.847 1.00 27.45
	ATOM	1774	CA GLN	428	1.00 27.43
	MOTA	1775	CB GLN	428	12.653 32.399 -4.942 1.00 29.19 11.247 32.108 -4.416 1.00 32.05
•	ATOM	1776	CG GLN	428	11.172 30.852 -3.561 1.00 36.92
30	ATOM ATOM	1777 1778	CD GLN	428	12.009 29.714 -4.139 1.00 39.47
00	ATOM	1779	OE1 GLN NB2 GLN	428 428	11.946 29.442 -5.345 1.00 41.41 12.788 29.034 -3.281 1.00 37.93
	ATOM	1780	C GLN	428	12 (54 22 52)
	ATOM	1781	O GLN	428	12.654 33.736 -5.675 1.00 28.90 12.466 33.780 -6.889 1.00 28.50
35	ATOM	1782	N VAL	429	12.844 34.826 -4.938 1.00 28.63
33	MOTA MOTA	1783 1784	CA VAL	429	12.893 36.145 -5.551 1.00 29.18
	MOTA	1785	CB VAL CG1 VAL	429 429	12.708 37.272 -4.515 1.00 29.49 12.789 38.632 -5.215 1.00 30.49
	ATOM	1786	CG2 VAL	429	11 202 27 105
40	ATOM	1787	C VAL	429	11.362 37.126 -3.824 1.00 30.87 14.260 36.297 -6.210 1.00 28.70
40	MOTA MOTA	1788	O VAL	429	14.398 36.924 -7.267 1.00 27.69
	ATOM	1789 1790	n Phe Ca Phe	430 430	15.279 35.723 -5.584 1.00 28.04
	ATOM	1791	CB PHE	430	16.601 35.793 -6.177 1.00 28.41 17.633 35.074 -5.317 1.00 27.09
45	MOTA	1792	CG PHE	430	17.633 35.074 -5.317 1.00 27.09 19.021 35.157 -5.872 1.00 27.44
45	ATOM	1793	CD1 PHE	430	19.777 36.314 -5.711 1.00 27.34
	ATOM ATOM	1794 1795	CD2 PHE CE1 PHE	430	19.553 34.096 -6.602 1.00 26.42
	ATOM	1796	CE1 PHE CE2 PHE	430 430	21.049 36.415 -6.274 1.00 27.80 20.807 34.182 -7.166 1.00 27.06
EΛ	MOTA	1797	CZ PHE	430	20.807 34.182 -7.166 1.00 27.06 21.564 35.346 -7.004 1.00 27.26
50	ATOM	1798	C PHE	430	16.549 35.120 -7.553 1.00 28.91
	ATOM ATOM	1799 1800	O PHE	430	17.104 35.641 -8.524 1.00 28.87
	ATOM	1801	N LYS CA LYS	431 431	15.886 33.964 -7.622 1.00 29.85 15.766 33.212 -8.874 1.00 32.68
	ATOM	1802	CB LYS	431	1.00 32.08
55	ATOM	1803	CG LYS	431	14.976 31.906 -8.670 1.00 33.56 14.832 31.090 -9.970 1.00 37.44
	ATOM	1804	CD LYS	431	13.617 30.145 -9.977 1.00 39.34
	ATOM ATOM	1805 1806	CE LYS NZ LYS	431	13.997 28.714 -9.618 1.00 41.84
	ATOM	1807	NZ LYS C LYS	431 431	14.937 28.127 -10.621 1.00 42.78 15.077 34.053 -9.944 1.00 33.57
60	MOTA	1808	O LYS	431	15.07/ 34.053 -9.944 1.00 33.57 15.415 33.958 -11.125 1.00 33.07
	ATOM	1809	n Gln	432	14.103 34.865 -9.536 1.00 34.34
	ATOM ATOM	1810 1811	CA GLN CB GLN	432	13.392 35.728 -10.484 1.00 35.91
	ATOM	1812	CB GLN CG GLN	432 432	12.353 36.589 -9.768 1.00 38.08 11.091 35.901 -9.303 1.00 39.88
65	MOTA	1813	CD GLN	432	10 10 10 10 10 10 10 10 10 10 10 10 10 1
	MOTA	1814	OE1 GLN	432	10.123 36.910 -8.684 1.00 41.50 10.388 37.471 -7.617 1.00 40.92
	ATOM	1815	NE2 GLN	432	9.011 37.170 -9.372 1.00 42.35
	ATOM ATOM	1816 1817	C GLN	432	14.362 36.676 -11.182 1.00 35.12
70	ATOM	1818	O GLN N SER	432 433	14.358 36.804 -12.408 1.00 35.26 15.180 37.347 -10.377 1.00 34 32
	ATOM	1819	CA SER	433	2,00 31.32
	ATOM	1820	CB SER	433	16.156 38.313 -10.868 1.00 34.30 16.608 39.220 -9.718 1.00 33.92
	ATOM	1821	OG SER	433	15.605 40.165 -9.392 1.00 35.35
<i>7</i> 5	MOTA MOTA	1822	C SER	. 433	17.386 37.707 -11.536 1.00 33.58
, 0	ATOM	1823 1824	O SER N HIS	433 434	17.948 38.298 -12.458 1.00 33.32
	ATOM	1825	CA HIS	434	17.809 36.537 -11.071 1.00 33.33 18.990 35.890 -11.635 1.00 34.01
	MOTA	1826	CB HIS	434	18.990 35.890 -11.635 1.00 34.01 20.184 36.077 -10.697 1.00 34.09
80	ATOM	1827	CG HIS	434	20.418 37.498 -10.299 1.00 34.93
JU	ATOM ATOM	1828	CD2 HIS	434	21.195 38.462 -10.849 1.00 35.03
	ATOM	1829 1830	ND1 HIS CE1 HIS	434 434	19.776 38.087 -9.232 1.00 35.41 20.147 39.351 -9.140 1.00 35.21
	ATOM	1831	NE2 HIS	434	20.147 39.351 -9.140 1.00 35.21 21.007 39.604 -10.110 1.00 36.62
0=	ATOM	1832	C HIS	434	18.771 34.405 -11.883 1.00 34.38
85	ATOM	1833	O HIS	434	19.341 33.561 -11.193 1.00 33.93
	MOTA	1834	n pro	435	17.938 34.064 -12.876 1.00 34.98

		•							
	ATOM	1835	CD	PRO	435	17.182	34 919	-13.805	1 00 25 01
	ATOM	1836	CA	PRO	435	17.689	32.550	-13.003	1.00 35.01
	ATOM	1837						-13.158	1.00 35.44
			CB	PRO	435	16.607		-14.237	1.00 35.29
=	ATOM	1838	CG	PRO	435	16.916	33.963	-14.962	1.00 35.40
5	MOTA	1839	С	PRO	435	18.915	31.882	-13.613	1.00 36.20
	MOTA	1840	0	PRO	435	19.122	30.758		1.00 35.55
	ATOM	1841	N	ASP	436	19.733		-14.481	
		1842							1.00 37.54
	MOTA		CA	ASP	436	20.919	31.785		1.00 40.08
10	MOTA	1843	CB	ASP	436	21.634	32.607	-16.058	1.00 42.72
10	MOTA	1844	CG	ASP	436	22.700	31.794	-16.803	1.00 45.95
	MOTA	1845	OD1		436	22.313	30.821	-17.497	
									1.00 46.29
	MOTA	1846	OD2		436	23.914	32.119	-16.695	1.00 47.67
	ATOM	1847	С	ASP	436	21.918	31.423		1.00 39.77
<b></b>	ATOM	1848	0	ASP	436	22.572	30.385	-13.966	1.00 39.96
15	MOTA	1849	N	ILE	437	22.042	32.270	-12.867	
	MOTA	1850	CA	ILE	437	22.972	31.999		1.00 39.31
								-11.775	1.00 38.61
	MOTA	1851	CB	ILE	437	23.096	33.227		1.00 39.13
	MOTA	1852	CG2	ILE	437	23.864	32.842	-9.547	1.00 39.06
	MOTA	1853	CG1	ILE	437	23.848	34.378	-11.491	1.00 39.49
20	ATOM	1854	CD1		437	23.124	34.982		
								-12.681	1.00 41.59
	ATOM	1855	C	ILE	437	22.538	30.757	-10.995	1.00 38.28
	MOTA	1856	0	ILE	437	23.350	29.858	-10.745	1.00 37.65
	MOTA	1857	N	VAL	438	21.255	30.692	-10.641	1.00 37.18
	ATOM	1858	CA	VAL	438	20.727	29.566	-9.885	
25	ATOM	1859	CB	VAL	438	19.239			1.00 37.56
							29.785	-9.458	1.00 37.27
	MOTA	1860		VAL	438	18.716	28.546	-8.751	1.00 36.25
	MOTA	1861	CG2	VAL	438	19.116	30.983	-8.525	1.00 36.28
	ATOM	1862	С	VAL	438	20.800	28.261	-10.672	1.00 38.30
	ATOM	1863	õ	VAL	438	21.265			
30								-10.157	1.00 37.66
50	ATOM	1864	Ŋ	ASN	439	20.368	28.287	-11.927	1.00 39.10
	ATOM	1865	CA	ASN	439	20.370	27.060	-12.716	1.00 39.91
	MOTA	1866	CB	ASN	439	19.390	27.189	-13.895	1.00 41.62
	ATOM	1867	CG	ASN	439	17.934	27.190	-13.445	
	MOTA	1868							1.00 43.36
35				ASN	439	17.596	26.609	-12.410	1.00 44.58
55	MOTA	1869	ND2		439	17.064	27.827	-14.225	1.00 44.62
	ATOM	1870	С	ASN	439	21.711	26.555	-13.219	1.00 39.39
	ATOM	1871	0	ASN	439	× 21.835	25.377	-13.561	1.00 40.93
	ATOM	1872	N	THR	440	22.728	27.406		
								-13.260	1.00 39.19
40	ATOM	1873	CA	THR	440	24.017	26.950	-13.777	1.00 38.65
40	ATOM	1874	CB	THR	440	24.287	27.533	-15.181	1.00 38.77
	MOTA	1875	OG1	THR	440	24.895	28.828	-15.057	1.00 40.00
	ATOM	1876	CG2		440	22.985	27.670	-15.955	
	ATOM	1877	c	THR	440	25.248			1.00 38.78
							27.238	-12.926	1.00 37.59
15	MOTA	1878	0	THR	440	26.353	26.835	-13.290	1.00 38.22
45	MOTA	1879	N	LEU	441	25.079	27.940	-11.811	1.00 35.62
•	MOTA	1880	CA	LEU	441	26.224	28.254	-10.965	1.00 33.88
	ATOM	1881	CB	LEU	441	26.494	29.762		
	ATOM							-10.971	1.00 35.57
		1882	CG	LEU	441	27.001	30.326	-12.304	1.00 37.86
EO .	MOTA	1883		LEU	441	27.177	31.837	-12.174	1.00 38.20
50	ATOM	1884	CD2	LEU	441	28.321	29.677	-12.683	1.00 38.80
	MOTA	1885	С	LEU	441	26.071	27.763	-9.533	1.00 31.60
	MOTA	1886	ō	LEU	441				
						27.064	27.532	-8.839	1.00 32.48
	ATOM	1887	N	PHE	442	24.831	27.602	-9.086	1.00 28.10
66	MOTA	1888	CA	PHE	442	24.587	27.122	-7.731	1.00 25.29
55	ATOM	1889	CB	PHE	442	23.135	27.405	-7.318	1.00 25.99
	ATOM	1890	CG	PHE	442	22.909	28.776		
	ATOM							-6.747	1.00 27.30
		1891		PHE .	442	23.833	29.796	-6.937	1.00 26.54
	ATOM	1892		PHE	442	21.748	29.047	-6.026	1.00 27.97
<b>~</b>	ATOM	1893	CE1	PHE	442	23.604	31.064	-6.416	1.00 29.09
60	ATOM	1894	CE2	PHE	442	21.508	30.321	-5.499	1.00 28.50
	ATOM	1895	CZ	PHE	442	22.438	31.326		
		1896						-5.695	1.00 27.97
	ATOM		C	PHE	442	24.830	25.615	-7.676	1.00 23.49
	ATOM	1897	0	PHE	442	24.616	24.907	-8.663	1.00 21.57
/-	ATOM	1898	N	PRO	443	25.300	25.107	-6.525	1.00 21.70
65	ATOM	1899	CD	PRO	443	25.758	25.819	-5.316	1.00 21.76
	ATOM	1900	CA	PRO	443	25.539			
							23.665	-6.414	1.00 21.30
	MOTA	1901	CB	PRO	443	25.886	23.488	-4.940	1.00 20.81
	ATOM	1902	CG	PRO	443	26.615	24.773	-4.619	1.00 20.63
	ATOM	1903	С	PRO	443	24.263	22.911	-6.795	1.00 22.58
70	ATOM	1904	Ō	PRO	443	23.179			
. •							23.243	-6.326	1.00 21.97
	MOTA	1905	N	PRO	444	24.377	21.893	-7.662	1.00 24.17
	MOTA	1906	CD	PRO	444	25.574	21.463	-8.404	1.00 24.11
	ATOM	1907	CA	PRO	444	23.205	21.117	-8.080	1.00 24.81
	ATOM	1908	СВ	PRO	444	23.825	19.970	-8.867	
<i>7</i> 5									1.00 25.10
, 0	ATOM	1909	CG	PRO	444	24.976	20.652	-9.543	1.00 25.51
	ATOM	1910	С	PRO	444	22.313	20.637	-6.933	1.00 24.27
	ATOM	1911	0	PRO	444	21.093	20.599	-7.081	1.00 24.40
	ATOM	1912	N	LEU	445	22.905	20.272	-5.797	
	ATOM	1913	CA						1.00 23.7B
80				LEU	445	22.106	19.807	-4.653	1.00 23.55
00	ATOM	1914	СВ	LEU	445	23.001	19.218	-3.563	1.00 22.47
	MOTA	1915	CG	LEU	445	22.273	18.815	-2.274	1.00 21.23
	MOTA	1916		LEU	445	21.251	17.742	-2.592	1.00 22.32
	ATOM	1917		LEU	445	23.273	18.307	-1.242	
									1.00 20.86
QE	ATOM	1918	C	LEU	445	21.278	20.943	-4.055	1.00 22.92
85	MOTA	1919	0	LEU	445	20.124	20.757	-3.647	1.00 21.21
	MOTA	1920	N	TYR	446	21.880	22.121	-3.998	1.00 23.10
									00 23.10

							~,		
	ATOM	1921	CA	TYR	446	21.19	7 23.2	94 3 46	
	ATOM	1922		TYR	446	22.17			
	ATOM	1923	CG	TYR	446	21.61			
5	ATOM	1924		TYR	446	20.89			
3	ATOM	1925		TYR	446	20.43	0 27.8		
	MOTA MOTA	1926		TYR	446	21.85			1.00 23.35
	MOTA	1927 1928	CE2	TYR TYR	446	21.39			2 1.00 25.61
	ATOM	1929	OH	TYR	446	20.68			
10	ATOM	1930	c.	TYR	446	20.28 19.98			
	ATOM	1931	ō	TYR	446	18.90			
	MOTA	1932	N	LYS	447	20.16			
	ATOM	1933	CA	LYS	447	19.06			
15	ATOM	1934	CB	LYS	447	19.56			
15	MOTA	1935	CG	LYS	447	18.45			
	ATOM	1936	CD	LYS	447	19.02			
	MOTA	1937	CE	LYS	447	17.92	0 23.59		
	ATOM	1938	NZ	LYS	447	18.49			1.00 40.17
20	ATOM	1939	C	LYS	447	17.98		_	1.00 25.88
20	ATOM ATOM	1940 1941	O N	LYS	447	16.79			
	ATOM	1942	CA	GLU GLU	448 448	18.41			
	ATOM	1943	CB	GLU	448	17.49			
	MOTA	1944	CG	GLU	448	18.29 17.44			
25	ATOM	1945	CD	GLU	448	18.23			
	ATOM	1946	OE1		448	18.78			
	ATOM	1947	OE2		448	18.30			
	MOTA	1948	С	GLU	448	16.63			1.00 30.84 1.00 26.51
20	MOTA	1949	0	GLU	448	15.43			1.00 26.31
30	ATOM	1950	N	LEU	449	17.26			1.00 25.93
	ATOM	1951	CA	LEU	449	16.589	20.98		1.00 26.71
	MOTA	1952	CB	LEU	449	17.622			1.00 26.21
	ATOM ATOM	1953	CG	LEU	449	18.502			1.00 26.61
35	ATOM	1954 1955	CD1		449	19.610			1.00 25.71
55	ATOM	1956	CD2 C	LEU	449	17.633			1.00 26.71
	ATOM	1957		LEU	449 449	15.674			1.00 28.16
	ATOM	1958		PHE	450	14.593			1.00 28.09
	ATOM	1959		PHE	450	15.338			1.00 29.00
40	ATOM	1960		PHE	450	16.224			1.00 31.20
	MOTA	1961		PHE	450	16.886			1.00 29.89 1.00 27.85
	ATOM	1962	CD1	PHE	450	18.263			1.00 27.85
	ATOM	1963	CD2	PHE	450	16.127			1.00 28.29
45	ATOM	1964	CE1		450	18.877			1.00 27.72
40	MOTA	1965	CE2		450	16.723	24.19		1.00 27.38
	MOTA	1966		PHE	450	18.105		5 1.518	1.00 28.09
	ATOM ATOM	1967 1968		PHE	450	14.625			1.00 33.41
	ATOM	1969		PHE ASN	450	13.844			1.00 32.89
50	ATOM	1970		ASN	451 451	14.889			1.00 36.22
	ATOM	1971		ASN	451	15.168			1.00 39.47
	ATOM	1972		ASN	451	15.939			1.00 41.40
	ATOM	1973	OD1		451	15.371			1.00 43.69
55	ATOM	1974	ND2	ASN	451	17.238			1.00 44.14 1.00 44.76
33	ATOM	1975		ASN	451	13.217			1.00 40.32
	ATOM	1976		ASN	451	11.993	24.72		1.00 41.43
	ATOM	1977		ASN	451	13.696		7 -7.475	1.00 40.86
	ATOM	1978		HIS	691	15.393			1.00 41.85
60	ATOM ATOM	1979		HIS	691	13.918			1.00 43.67
00	ATOM	1980 1981	CD2 I		691 691	13.151			1.00 44.45
	ATOM	1982	CE1		691	13.051			1.00 44.92
	ATOM	1983	NE2		691	11.810 11.843	13.358 14.629		1.00 45.35
<b></b>	ATOM	1984		IIS	691	16.996	13.164		1.00 45.49
65	MOTA	1985		IIS	691	17.471	12.469		1.00 38.01 1.00 38.13
	MOTA	1986	N I	iis	691	14.685	13.691		1.00 38.13
	ATOM	1987	CA I	iis	691	15.813	14.063		1.00 39.14
	ATOM	1988	N I	LYS	692	17.475	13.190		1.00 36.76
70	MOTA	1989		LYS	692	18.589	12.350		1.00 35.59
70	ATOM	1990		YS	692	18.893	12.623		1.00 37.83
	MOTA	1991		YS	692	19.742	11.564	-10.051	1.00 40.63
	ATOM	1992		YS	692	19.728	11.714		1.00 42.76
	MOTA MOTA	1993 1994		YS	692	20.323	10.472		1.00 43.47
<i>7</i> 5	MOTA	1995		YS	692	21.706	10.196		1.00 43.90
, ,	MOTA	1996		YS	692	19.873	12.498		1.00 33.87
	ATOM	1997		YS LE	692 693	20.467	11.509		1.00 33.35
	MOTA	1998		LE	693 693	20.309	13.729		1.00 32.23
0.0	MOTA	1999		LE	693	21.535 21.930	13.950		1.00 31.32
80	ATOM	2000	CG2 I		693	23.269	15.427 15.635		1.00 30.80
-	ATOM	2001	CG1 I		693	22.033	15.873		1.00 29.72
	ATOM	2002	CD1 I		693	22.234	17.371	-7.508 -7.780	1.00 31.13 1.00 31.56
	ATOM	2003		LE	693	21.432	13.482		1.00 30.60
QE	ATOM	2004	0 1	LE	693	22.298	12.750	-4.201	1.00 30.47
85	MOTA	2005		EU	694	20.373	13.894	-3.988	1.00 30.60
	MOTA	2006	CA L	Eυ	694	20.189	13.498	-2.599	1.00 29.95

	MOTA	2007	CB LEU	694	18.901	14.127	-2.049	1.00 30.02
	ATOM	2008	CG LEU		18.575			
						13.956	-0.565	1.00 30.42
	ATOM	2009	CD1 LEU		19.761	14.380	0.289	1.00 27.83
_	ATOM	2010	CD2 LEU	1 694	17.338	14.782	-0.228	1.00 29.11
5	MOTA	2011	C. TEI	694	20.133	11.973	-2.530	1.00 31.03
	ATOM	2012	O LEU		20.692	11.347	-1.624	1.00 28.47
	MOTA	2013	N HIS		19.476	11.365		
							-3.512	1.00 31.88
	ATOM	2014	CA HIS		19.374	9.913	-3.529	1.00 33.30
40	MOTA	2015	CB HIS	695	18.477	9.459	-4.670	1.00 36.30
10	MOTA	2016	CG HIS	695	17.945	8.080	-4.478	1.00 40.00
	ATOM	2017	CD2 HIS		16.683	7.629	-4.299	
	ATOM	2018	ND1 HIS					1.00 41.54
					18.768	6.980	-4.364	1.00 41.93
	MOTA	2019	CE1 HIS		18.035	5.910	-4.117	1.00 42.57
	ATOM	2020	NE2 HIS	695	16.766	6.277	-4.071	1.00 43.22
15	MOTA	2021	C HIS	695	20.746	9.260	-3.676	1.00 33.11
	ATOM	2022	O HIS		21.048	8.249	-3.040	
	MOTA		N ARG					1.00 32.39
		2023			21.579	9.849	-4.521	1.00 32.29
	ATOM	2024	CA ARG		22.909	9.322	-4.743	1.00 30.93
	MOTA	2025	CB ARG	696	23.603	10.093	-5.867	1.00 31.23
20	ATOM	2026	CG ARG	696	24.984	9.543	-6.182	1.00 32.75
	ATOM	2027	CD ARG		25.804	10.477	-7.050	
								1.00 33.56
	ATOM	2028	NE ARG		27.125	9.909	-7.307	1.00 35.72
	MOTA	2029	CZ ARG		28.099	10.546	-7.950	1.00 35.45
0.5	MOTA	2030	NH1 ARG	696	27.901	11.782	-8.398	1.00 35.32
25	MOTA	2031	NH2 ARG	696	29.268	9.943	-8.151	1.00 36.04
	ATOM	2032	C ARG		23.772	9.386	-3.480	1.00 29.89
	ATOM	2033	O ARG					
					24.475	8.433	-3.161	1.00 29.24
	ATOM	2034	N LEU		23.716	10.509	~2.768	1.00 29.17
20	MOTA	2035	CA LEU		24.511	10.690	-1.557	1.00 28.52
30	MOTA	2036	CB LEU	697	24.368	12.124	-1.046	1.00 26.92
	MOTA	2037	CG LEU	697	24.699	13.228	-2.053	1.00 27.27
	ATOM	2038	CD1 LEU		24.463			
						14.602	-1.417	1.00 25.02
	ATOM	2039	CD2 LEU		26.142	13.085	-2.505	1.00 26.53
25	MOTA	2040	C LEU		24.140	9.712	-0.448	1.00 29.70
35	MOTA	2041	O LEU	697	25.004	9.258	0.302	1.00 28.66
	ATOM	2042	N LEU	698	22.853	9.397	-0.345	1.00 31.41
	MOTA	2043	CA. LEU		22.375	8.453	0.661	1.00 34.12
	ATOM	2044	CB LEU		20.846			
						8.472	0.718	1.00 33.23
40	MOTA	2045	CG LEU		20.134	9.426	1.669	1.00 32.91
<b>4</b> 0	MOTA	2046	CD1 LEU		18.680	9.463	1.307	1.00 33.90
	MOTA	2047	CD2 LEU	698	20.302	8.964	3.107	1.00 31.41
	MOTA	2048	C LEU	698	22.848	7.044	0.315	1.00 36.29
	MOTA	2049	O LEU		23.159	6.242	1.194	
	ATOM	2050	N GLN	699				1.00 36.31
45					22.909	6.760	-0.977	1.00 39.15
40	ATOM	2051	CA GLN		23.328	5.450	-1.471	1.00 42.12
	MOTA	2052	CB GLN	699	22.802	5.239	-2.896	1.00 43.64
	MOTA	2053	CG GLN	699	21.274	5.140	-2.989	1.00 45.98
	ATOM	2054	CD GLN	699 ·	20.750	3.781	-2.547	1.00 47.08
_	ATOM	2055	OE1 GLN	699	21.233	3.204	-1.566	1.00 48.60
50	ATOM	2056	NE2 GLN	699	19.747	3.269		
00							-3.258	1.00 48.36
	MOTA	2057	C GLN	699	24.836	5.245	-1.465	1.00 43.37
	MOTA	2058	O GLN	699	25.305	4.126	-1.660	1.00 43.65
	ATOM	2059	N GLU	700	25.599	6.312	-1.260	1.00 44.64
	ATOM	2060	CA GLU	700	27.052	6.190	-1.250	1.00 47.04
55	ATOM	2061	CB GLU	700	27.700	7.568	-1.095	1.00 47.40
	ATOM	2062	CG GLU	700	29.220			
						7.519	-1.157	1.00 49.39
	ATOM	2063	CD GLU	700	29.791	8.048	-2.461	1.00 49.85
	ATOM	2064	OE1 GLU	700	29.268	7.680	-3.554	1.00 49.19
<b>60</b>	ATOM	2065	OE2 GLU	700	30.763	8.836	-2.382	1.00 51.58
60	ATOM	2066	C GLU	700	27.540	5.255	-0.132	1.00 48.52
	MOTA	2067	O GLU		28.449	4.423	-0.386	1.00 48.99
	ATOM	2068	OXT GLU		27.021	5.379	1.001	
	ATOM	2069	OH2 WAT	801				1.00 49.57
					14.817	26.937	2.587	1.00 20.16
<b>6</b> E	ATOM	2070	OH2 WAT	802	26.733	20.689	8.917	1.00 19.93
65	ATOM	2071	OH2 WAT	803	26.566	41.076	13.914	1.00 25.96
	MOTA	2072	OH2 WAT	804	12.901	16.692	8.722	1.00 19.78
	ATOM	2073	OH2 WAT	805	21.441	41.033	3.838	1.00 27.88
	ATOM	2074	OH2 WAT	806	11.576	19.809		
							13.280	1.00 21.67
70	ATOM	2075	OH2 WAT	807	24.269	17.527	14.566	1.00 22.47
70	ATOM	2076	OH2 WAT	808	25.329	19.487	-5.550	1.00 38.43
	MOTA	2077	OH2 WAT	809	28.090	41.701	1.977	1.00 27.58
	ATOM '	2078	OH2 WAT	810	1.405	9.268	4.014	1.00 28.13
	ATOM	2079	OH2 WAT	811	7.275	28.248	11.748	1.00 33.78
	ATOM	2080	OH2 WAT					
<i>7</i> 5				812	24.068	26.427	23.332	1.00 29.89
/ )	MOTA	2081	OH2 WAT	813	14.772	34.264	14.684	1.00 25.08
	ATOM	2082	OH2 WAT	814	12.543	3.741	17.005	1.00 29.72
	ATOM	2083	OH2 WAT	815	30.580	18.289	2.261	1.00 31.66
	MOTA	2084	OH2 WAT	816	36.688	39.061	2.238	1.00 31.61
	ATOM	2085	OH2 WAT	817	11.630	23.199		
80							6.840	1.00 31.07
00	ATOM	2086	OH2 WAT	818	2.742	5.405	10.288	1.00 30.11
	ATOM	2087	OH2 WAT	819	1.368	13.915	5.083	1.00 35.24
	MOTA	2088	OH2 WAT	820	3.546	13.308	8.739	1.00 32.87
	ATOM	2089	OH2 WAT	821	0.197	11.314	7.692	1.00 31.34
	ATOM	2090	OH2 WAT	822	-0.265	12.324	3.836	1.00 31.56
85	ATOM	2091	OH2 WAT	823	32.317	41.732		
50							11.781	1.00 30.31
	MOTA	2092	OH2 WAT	824	31.188	22.170	11.656	1.00 30.40

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	ATOM	2093	OH2 WAT	825	28.708 24.054 13.003 1.00 32.74
	MOTA	2094		826	30.451 24.872 11.210 1.00 53.39
	MOTA MOTA	2095 2096		832	14.659 19.191 30.954 1.00 33.74
5	ATOM	2097		835 836	2.458 12.055 6.762 1.00 30.04 8.996 22.689 12.009 1.00 49.90
	ATOM	2098		837	8.996 22.689 12.009 1.00 49.90 14.375 24.499 4.186 1.00 30.61
	ATOM	2099		839	2.130 4.386 7.857 1.00 30.22
	ATOM ATOM	2100 2101	OH2 WAT	840	26.339 16.316 27.739 1.00 35.01
10	ATOM	2102	OH2 WAT	841 842	8.001 21.050 7.844 1.00 25.09 11.218 3.956 14.667 1.00 29 78
	ATOM	2103	OH2 WAT	843	11.218 3.956 14.667 1.00 29.78 13.538 3.582 13.108 1.00 29.55
	MOTA	2104	OH2 WAT	844	12.401 22.827 13.222 1.00 30.20
	MOTA MOTA	2105	OH2 WAT	846	34.979 40.443 11.829 1.00 38.06
15	ATOM	2106 2107	OH2 WAT OH2 WAT	847 848	9.388 6.952 8.514 1.00 44.86 9.424 32.516 7.968 1.00 34.80
	ATOM	2108	OH2 WAT	849	9.424 32.516 7.968 1.00 34.80 12.152 25.422 5.217 1.00 33.49
	ATOM	2109	OH2 WAT	850	38.479 45.718 1.108 1.00 32.54
	MOTA ATOM	2110 2111	OH2 WAT	851	32.489 27.280 7.768 1.00 52.84
20	ATOM	2112	OH2 WAT OH2 WAT	852 853	19.651 17.055 -9.301 1.00 37.88 18.746 43.921 3.425 1.00 36.94
	MOTA	2113	OH2 WAT	854	18.746 43.921 3.425 1.00 36.94 25.431 10.057 28.150 1.00 38.06
	ATOM	2114	OH2 WAT	855	7.134 18.540 4.931 1.00 63.81
	ATOM ATOM	2115 2116	OH2 WAT	856	9.614 18.288 18.085 1.00 35.99
25	ATOM	2117	OH2 WAT	857 858	9.960 11.674 24.894 1.00 34.82 21.673 44.846 2.726 1.00 29.09
	MOTA	2118	OH2 WAT	859	21.673 44.846 2.726 1.00 29.09 12.420 -0.591 5.172 1.00 56.22
	MOTA	2119	OH2 WAT	860	2.112 7.553 21.676 1.00 63.50
	ATOM ATOM	2120 2121	OH2 WAT OH2 WAT	861	32.871 18.504 18.445 1.00 37.53
30	ATOM	2122	OH2 WAT	862 863	7.060 24.628 6.457 1.00 41.11 30.339 19.808 24.562 1.00 35.73
	MOTA	2123	OH2 WAT	865	30.339 19.808 24.562 1.00 35.73 31.408 40.456 -6.981 1.00 28.87
	ATOM	2124	OH2 WAT	866	16.060 42.941 9.793 1.00 44.24
	ATOM ATOM	2125 2126	OH2 WAT	867 868	12.843 26.219 0.918 1.00 35.68
35	ATOM	2127	OH2 WAT	869	37.364 44.144 -7.616 1.00 64.48 8.875 20.108 12.516 1.00 35.65
	MOTA	2128	OH2 WAT	870	15.439 22.492 5.981 1.00 34.94
	ATOM	2129	OH2 WAT	871	23.795 42.644 6.558 1.00 37.44
	ATOM ATOM	2130 2131	OH2 WAT OH2 WAT	873 874	24.777 38.088 21.937 1.00 37.38 19.791 35.055 -15.004 1.00 49.00
<b>4</b> 0	ATOM	2132	OH2 WAT	875	19.791 35.055 -15.004 1.00 49.00 4.885 20.278 10.170 1.00 42.95
	MOTA	2133	OH2 WAT	876	22.387 24.643 -10.436 1.00 51.01
	ATOM ATOM	2134 2135	OH2 WAT	877	12.606 26.960 -1.579 1.00 38.28
	ATOM	2136	OH2 WAT	878 879	29.020 8.186 21.464 1.00 34.65 19.154 5.255 15.898 1.00 45.06
<b>4</b> 5	MOTA	- 2137	OH2 WAT	880	19.154 5.255 15.898 1.00 45.06 23.704 47.324 18.452 1.00 68.34
	ATOM	2138	OH2 WAT	881	28.057 9.062 6.603 1.00 44.32
	ATOM ATOM	2139 2140	OH2 WAT OH2 WAT	883 884	43.023 41.890 5.788 1.00 38.31
<b>50</b>	MOTA	2141	OH2 WAT	885	7.119 28.891 9.099 1.00 32.09 17.021 2.408 2.764 1.00 45.47
.50	MOTA	2142	OH2 WAT	886	23.215 4.005 10.105 1.00 32.13
	ATOM ATOM	2143 2144	OH2 WAT	887	15.983 38.039 -2.715 1.00 54.73
	MOTA	2145	OH2 WAT OH2 WAT	889 890	4.205 3.441 11.079 1.00 39.06 20.791 9.054 -7.915 1.00 33.22
<b>F F</b>	ATOM	2146	OH2 WAT	891	20.791 9.054 -7.915 1.00 33.22 25.305 7.602 26.964 1.00 51.43
55	ATOM	2147	OH2 WAT	892	27.413 6.919 14.503 1.00 32.31
	ATOM ATOM	2148 2149	OH2 WAT OH2 WAT	893 894	33.552 15.908 12.742 1.00 47.40 27.172 23.883 29.442 1.00 51 19
	ATOM	2150	OH2 WAT	895	27.172 23.883 29.442 1.00 51.19 32.219 29.350 18.302 1.00 39.52
60	ATOM	2151	OH2 WAT	896	20.082 1.162 10.052 1.00 37.15
60	MOTA MOTA	2152 2153	OH2 WAT	898	23.983 4.384 5.989 1.00 35.18
	ATOM	2154	OH2 WAT OH2 WAT	899 900	9.782 19.780 0.976 1.00 50.23 36.407 19.082 20.876 1.00 44.97
	ATOM	2155	OH2 WAT	901	7.403 19.567 14.815 1.00 37.37
65	MOTA	2156	OH2 WAT	902	39.710 36.772 1.207 1.00 58.27
03	ATOM ATOM	2157 2158	OH2 WAT OH2 WAT	903	10.185 18.360 15.457 1.00 33.56
	ATOM	2159	OH2 WAT	904 905	10.260 38.244 11.664 1.00 51.98 11.584 31.849 -8.614 1.00 37.52
	ATOM	2160	OH2 WAT	906	31.638 29.686 -0.266 1.00 32.48
<i>7</i> 0 .	ATOM	2161	OH2 WAT	907	-0.206 4.924 11.081 1.00 36.49
/0 .	ATOM ATOM	2162 2163	OH2 WAT	908	31.665 29.237 6.272 1.00 49.19
	MOTA	2164	OH2 WAT	909 910	-2.417 16.800 9.041 1.00 44.02 10.940 39.261 6.571 1.00 43.92
	MOTA	2165	OH2 WAT	911	10.940 39.261 6.571 1.00 43.92 13.036 1.866 1.304 1.00 40.13
75	ATOM	2166	OH2 WAT	912	14.565 2.593 15.801 1.00 47.21
/3	ATOM ATOM	2167 2168	OH2 WAT	913	15.968 17.289 31.561 1.00 33.25
	ATOM	2169	OH2 WAT OH2 WAT	914 915	34.332 36.096 17.436 1.00 48.32 -0.731 12.520 9.973 1.00 49.45
	ATOM	2170	OH2 WAT	916	-0.731 12.520 9.973 1.00 49.45 19.666 1.578 18.349 1.00 44.84
80	MOTA	2171	OH2 WAT	917	22.978 40.125 16.179 1.00 45.10
50	ATOM ATOM	2172 2173	OH2 WAT OH2 WAT	918 919	14.785 33.819 17.497 1.00 38.88
	ATOM	2174	OH2 WAT	920	25.871 13.595 -7.644 1.00 45.77 25.570 6.591 -4.596 1.00 38.57
	MOTA	2175	OH2 WAT	921	16.974 2.870 16.605 1.00 33.05
85	ATOM	2176	OH2 WAT	922	33.181 45.831 10.253 1.00 42.64
00	ATOM ATOM	2177 2178	OH2 WAT OH2 WAT	923 924	12.975 32.550 -12.651 1.00 46.09 26.965 45.895 0.183 1.00 55.12
	🕶	-1,0		767	26.965 45.895 0.183 1.00 55.12

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2179
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                      OH2 WAT
                                                     22.836
                                                              18.961
                                 925
                                             7.626
                                                                       1.00 41.09
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                          WAT
                                 926
927
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                          WAT
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                                            18.916
                                                     35.911
                                                             -17.290
                                                                       1.00 54.56
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                      OH2
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                                             7.922
                                                     23.555
                                                              24.917
                                                                       1.00 41 77
                          WAT
                                 932
933
                                           22.938
34.983
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                                                             21.176
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                      OH2
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10
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               2188
                          WAT
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                                                     29.254
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17.800
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                          WAT
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                          WAT
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15
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                                                               4.335
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                          WAT
                                 944
                                            26.414
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                      OH2
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       MOTA
               2198
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                                                                       1.00 32.92
1.00 53.88
       MOTA
               2199
                      OH2
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                          WAT
       ATOM
               2200
                      OH2
                                 950
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                                                     22.869
                                                               6.573
                                                                       1.00 38.42
                          WAT
       ATOM
               2201
                                 951
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               2202
                      OH2
                          WAT
                                 952
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7.254
                                                                       1.00 36.76
25
                          WAT
       ATOM
               2203
                      OH2
                                 954
                                           34.805
                                                     28.111.
                                                                       1.00 38.30
       ATOM
               2204
                      OH2
                          WAT
                                 955
                                            19.872
                                                     20.234
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                      OH2
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                                           28.707
                                                     27.099
                                                              7.452
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C5
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       MOTA
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22.034
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                      C12 STE
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45
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                                                              7.586
                                                                      1.00 42.74
       MOTA
               2224
                      C18
                          STE
                                1001
                                           22.227
                                                     28.387
                                                              8.831
                                                                      1.00
       ATOM
                      C3
                          STE
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                                           27.878
                                                    26.507
                                                              8.311
                                                                      1.00 50.33
       END
50
       TABLE B: Crystallographic Coordinates of RORbeta
```

LBD/retinoic acid/SRC1 peptide complex

```
MOTA
                                                    -1.893
-2.232
                     СВ
                          THR
                                           14.936
                                                             26.570
                                                                      1.00 44.08
       ATOM
                     OG1 THR
                                           16.329
                                                             26.551
                                                                      1.00 44.42
55
       ATOM
                     CG2
                          THR
                                   1
                                           14.475
                                                     -1.471
                                                                      1.00 44.84
                                                             25.180
       MOTA
                     С
                          THR
                                   1
                                           15.825
                                                     0.265
                                                             27.508
                                                                      1.00 44.25
       MOTA
                     0
                          THR
                                   1
                                           16.183
                                                     0.740
                                                             26.428
                                                                      1.00 42.75
       ATOM
                  6
                     N
                          THR
                                           13.347
                                                    -0.138
                                                             27.331
                                                                      1.00 43.63
       MOTA
                     CA
                          THR
                                   1
                                           14.685
                                                    -0.761
                                                             27.580
                                                                      1.00 44.30
60
                                                             28.670
       ATOM
                  R
                     N
                          MET
                                           16.388
                                                     0.599
                                                                      1.00 44.87
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       ATOM
                  9
                     CA
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                                           17,474
                                                     1.576
                                                             28.770
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                 10
                     ÇВ
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                                           19.927
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                                                             26.793
                                                                      1.00 40.28
       ATOM
                 19
                     OG
                          SER
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                                                             25.874
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                     С
                          SER
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                                                             24.883
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75
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                     CD
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                                                             21.124
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80
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                          GLU
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       ATOM
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                                                     2.552
                                                             22.674
                                                                      1.00 33.90
```

 $A = A_{ij}$ 

Ξ,

				51		•
	ATOM	31 N ILE	5	18.010 2.	661 24.511	1 1.00 31.72
	ATOM	32 CA ILE	5	18.099 4.	112 24.600	
	MOTA ATOM	33 CB ILE	5		654 25.856	1.00 31.04
5	ATOM	34 CG2 ILE 35 CG1 ILE	5 5		169 25.921	
_	ATOM	36 CD1 ILE	5		272 25.828 371 24.668	
	MOTA	37 C ILE	5		547 24.640	
	ATOM	38 O ILE	5		167 23.939	
10	MOTA	39 N ASP	6		376 25.458	1.00 31.69
10	MOTA MOTA	40 CA ASP 41 CB ASP	6 6		27 25.567	
	ATOM	42 CG ASP	6	23.900 3.8	137 26.706 307 26.898	
	ATOM	43 OD1 ASP	6	24.241 5.0		
15	ATOM	44 OD2 ASP	6	24.711 2.9		
15	MOTA	45 C ASP	6	22.524 3.9	99 24.256	
	ATOM ATOM	46 O ASP 47 N ARG	6 7	23.303 4.8		1.00 30.34
	MOTA	47 N ARG 48 CA ARG	7.	22.298 2.8 22.992 2.5		
-00	MOTA	49 CB ARG	ż	22.675 1.1		· <del>-</del> ·
20	MOTA	50 CG ARG	7	23.169 0.0		
	ATOM	51 CD ARG	7	22.770 -1.2		1.00 48.39
	ATOM	52 NE ARG	7	21.346 -1.3		
	ATOM ATOM	53 CZ ARG 54 NH1 ARG	7 7	20.751 -2.3		1.00 52.86
25	ATOM	55 NH2 ARG	7.	21.456 -3.3 19.454 -2.2		1.00 54.84
	ATOM	56 C ARG	7	22.620 3.6		1.00 54.02
	MOTA	57 O ARG	7	23.487 4.1		1.00 30.15 1.00 29.79
	MOTA	58 N ILE	8	21.332 3.9		1.00 28.75
30	ATOM	59 CA ILE	8	20.865 4.9		1.00 27.58
50	ATOM ATOM	60 CB ILE 61 CG2 ILE	8	19.330 5.1		1.00 26.92
*	ATOM	62 CG1 ILE	8 8	18.917 6.4 18.589 3.9	_	1.00 24.05
	ATOM	63 CD1 ILE	8	17.065 4.0		1.00 28.50 1.00 25.10
25	ATOM	64 C ILE	8	21.571 6.2		1.00 28.49
35	ATOM	65 O ILE	8	22.081 6.9		1.00 27.22
	ATOM ATOM	66 N ALA 67 CA ALA	9	21.600 6.6		1.00 28.38
	ATOM	67 CA ALA 68 CB ALA	9 9	22.241 7.9 22.086 8.1		1.00 28.28
40	ATOM	69 C ALA	ğ	22.086 8.1 23.721 7.9		1.00 26.41
40	MOTA	70 O ALA	9	24.176 8.8		1.00 29.29 1.00 27.81
	ATOM	71 N GLN	10	24.474 6.9		1.00 30.09
	ATOM ATOM	72 CA GLN 73 CB GLN	10	25.897 6.8		1.00 30.31
	ATOM	73 CB GLN 74 CG GLN	10 10	26.515 5.58		1.00 34.96
45	ATOM	75 CD GLN	10	26.435 5.40 27.020 4.0		1.00 41.16
	MOTA	76 OE1 GLN	10	28.217 3.80		1.00 47.78 1.00 48.59
	ATOM	77 NE2 GLN	10	26.171 3.22		1.00 51.11
	ATOM ATOM	78 C GLN 79 O GLN	10	26.141 6.9		1.00 28.54
50	ATOM	79 O GLN 80 N ASN	10 11	27.031 7.60 25.350 6.22		1.00 29.98
	ATOM	81 CA ASN	11	25.350 6.22 25.486 6.21		1.00 26.39
	ATOM	82 CB ASN	11	24.439 5.20		1.00 25.48 1.00 25.98
	ATOM	83 CG ASN	11	24.439 5.29		1.00 24.40
55	ATOM ATOM	84 OD1 ASN	11	23.422 5.52		1.00 26.44
00	ATOM	85 ND2 ASN 86 C ASN	11 11	25.578 4.92 25.329 7.62	_	1.00 24.88
	ATOM	87 O ASN	11	25.329 7.62 26.106 8.04		1.00 25.80
	ATOM	88 N ILE	12	24.326 8.36		1.00 25.13 1.00 25.44
60	ATOM	89 CA ILE	12	24.092 9.71		1.00 24.85
OU	ATOM	90 CB ILE	12	22.743 10.25		1.00 23.12
	ATOM ATOM	91 CG2 ILE 92 CG1 ILE	12 12	22.617 11.73		1.00 22.76
	ATOM	93 CD1 ILE	12	21.613 9.46 20.253 9.76		1.00 23.39
<b>C</b> F	ATOM	94 C ILE	12	25.214 10.66		1.00 20.56 1.00 25.34
65	MOTA	95 O ILE	12	25.683 11.47		1.00 25.18
	ATOM	96 N ILE	13	25.648 10.55	6 19.198	1.00 25.76
	ATOM ATOM	97 CA ILE 98 CB ILE	13	26.728 11.40		1.00 26.18
	ATOM	98 CB ILE 99 CG2 ILE	13 13	26.993 11.13		1.00 26.42
70	ATOM	100 CG1 ILE	13	28.317 11.75 25.822 11.68		1.00 27.88
	ATOM	101 CD1 ILE	13	25.887 11.34		1.00 24.88 1.00 24.90
	ATOM	102 C ILE	13	27.987 11.12	2 18.855	1.00 26.22
	MOTA	103 O ILE	13	28.680 12.04	5 18.423	1.00 25.36
<i>7</i> 5	ATOM ATOM	104 N LYS	14	28.266 9.84		1.00 27.79
	ATOM	105 CA LYS 106 CB LYS	14 14	29.425 9.45 29.504 7.92		1.00 28.58
	ATOM	107 CG LYS	14	29.504 7.92 30.610 7.38		1.00 31.83
	ATOM	108 CD LYS	14	30.454 5.87		1.00 36.77 1.00 41.46
90	ATOM	109 CE LYS	14	31.523 5.32		1.00 42.19
80	ATOM	110 NZ LYS	14	32.877 5.44	9 16.278	1.00 44.14
	ATOM	111 C LYS	14	29.311 10.03	9 16.412	1.00 28.52

	ATOM	112	O LY	. 14	20	260	10 600	15 000	1 00	20.00
		113				. 268	10.609	15.883		29.83
	ATOM		N SE			.136	9.905	15.806		26.79
	ATOM	114	CA SE			929	10.429	14.459	1.00	26.88
_	MOTA	115	CB SE			500	10.132	13.994	1.00	27.05
5	MOTA	116	OG SE			280	10.611	12.676	1.00	30.56
	MOTA	117	C SE			193	11.932	14.414	1.00	26.19
	MOTA	118	O SE	R 15		. 895	12.427	13.529	1.00	25.81
	ATOM	119	N HI	S 16	27.	627	12.657	15.373	1.00	25.25
	MOTA	120	CA HI	S 16	27.	807	14.104	15.448	1.00	25.35
10	MOTA	121	CB HI	5 16	27.	098	14.652	16.688		23.98
	MOTA	122	CG HI	s 16	27.	485	16.055	17.035		22.83
	ATOM	123	CD2 HI			473	16.533	17.830		22.89
	MOTA	124	ND1 HI			831	17.159	16.530		21.54
	ATOM	125	CE1 HI			398	18.256	16.999		23.79
15	MOTA	126	NE2 HI			398	17.904	17.789		
10						296	14.438			24.95
	ATOM	127	C HI			794		15.532		27.00
	MOTA	128	O HI				15.325	14.832		25.20
	MOTA	129	N LE			998	13.723	16.406		27.86
20	MOTA	130	CA LE			423	13.940	16.591		28.80
20	ATOM	131	CB LE			996	12.917	17.578	1.00	30.56
	MOTA	132	CG LE	J 17		501	13.008	17.863	1.00	33.43
	MOTA	133	CD1 LE	J 17	33.	784	14.232	18.725	1.00	35.11
	MOTA	134	CD2 LE	J 17	33.	968	11.757	18.578	1.00	35.02
	. ATOM	135	C LE	J 17	32.	153	13.809	15.269	1.00	28.50
25	ATOM	136	O LE	J 17	33.	060	14.588	14.973		29.06
	ATOM	137	N GL		31.	758	12.833	14.466		27.38
	ATOM	138	CA GL			430	12.584	13.197		29.19
	ATOM	139	CB GL			419	11.080	12.897	1.00	30.86
	ATOM	140	CG GL			740	10.192	14.093		35.14
30	ATOM	141	CD GL			508	8.718	13.807		
50	ATOM	142	OE1 GL			604	8.399	12.997		38.27
										40.84
	ATOM	143	OE2 GL			215	7.877	14.407		38.21
	MOTA	144	C GL			884	13.311	11.977		28.77
35	MOTA	145	O GL			495	13.242	10.909		29.35
33	MOTA	146	N TH			767	14.023	12.109		26.26
	ATOM	147	CA TH			194	14.656	10.926		25.75
	ATOM	148	CB TH			916	13.921	10.510	1.00	24.77
	MOTA	149	OG1 TH			906	14.120	11.508	1.00	22.37
40	MOTA	150	CG2 TH	R 19	29.	194	12.428	10.366	1.00	24.32
40	MOTA	151	C TH	R 19	29.	888	16.148	10.903	1.00	26.21
	ATOM	152	O TH	R 19	29.	143	16.606	10.040	1.00	26.97
	MOTA	153	N CY	3 20	30.	425	16.916	11.839		28.90
	ATOM	154	CA CY	3 20	30.	190	18.351	11.789		31.93
	ATOM	155	CB CY			306	18.979	13.175		29.90
45	ATOM	156	SG CY			844	18.742	14.175		30.72
	ATOM	157	C CY			258	18.930	10.876		33.01
	ATOM	158	O CY			368	18.412	10.824	1.00	33.41
	ATOM	159	N GL			927	19.986	10.143		34.90
	MOTA	160	CA GL			911	20.595	9.261		
50	MOTA	161	CB GL			314	21.782	8.509	1.00	36.25
50		162				359	22.563			37.23
	ATOM							7.731		39.86
	ATOM	163	CD GL			797	23.770	7.024	1.00	39.83
	ATOM	164	OE1 GL			545	24.580	6.476		43.69
55	MOTA	165	NE2 GL			478	23.900	7.025		41.69
33	ATOM	166	C .GL			090	21.077	10.099		36.79
	ATOM	167	O GL			229	21.077	9.636		36.87
	MOTA	168	N TY			799	21.489	11.331		35.98
	ATOM	169	CA TY			818	21.974	12.262	1.00	37.06
<b>70</b>	MOTA	170	CB TY		33.	608	23.460	12.559	1.00	37.63
60	MOTA	171	CG TY	R 22	34.	105	24.384	11.480	1.00	37.76
	MOTA	172	CD1 TY	R 22	35.	467	24.505	11.219	1.00	39.21
	ATOM	173	CE1 TY	R 22	35.	933	25.362	10.231		41.19
	ATOM	174	CD2 TY			217	25.142	10.724		38.25
	MOTA	175	CE2 TY			671	26.001	9.733		40.65
65	ATOM	176	CZ TY			029	26.105	9.492		40.42
••	ATOM	177	OH TY			483	26.946	8.509		43.37
		178	C TY			786	21.214	13.580		
	MOTA					767	21.199			35.92
	ATOM	179	O TY					14.268		35.59
70	ATOM	180	N TH			900	20.587	13.935		36.10
70	ATOM	181	CA TH			968	19.861	15.193		36.94
	MOTA	182	CB TH			179	18.921	15.242		39.58
	ATOM	183	OG1 TH				19.700	15.216		39.59
	ATOM	184	CG2 TH			169	17.969	14.056	1.00	40.40
	ATOM	185	C TH	R 23	35.	128	20.892	16.302	1.00	36.49
<i>7</i> 5	MOTA	186	O TH	R 23	35.	459	22.052	16.041	1.00	32.29
	ATOM	187	N ME		34.	895	20.471	17.539		37.33
	ATOM	188	CA ME			029	21.371	18.674		38.75
	ATOM	189	CB ME			654	20.648	19.966		39.75
	ATOM	190	CG ME			161	20.570	20.204		42.25
80	ATOM	191	SD ME			471	22.130	20.821		43.80
-0		192	CE ME			356	23.099	19.341		43.48
	ATOM	174	CD ME	. 44	52.				1.00	

				· · · · · · · · ·
	MOTA	193 C MET	24	36.454 21.889 18.765 1.00 39.58
	ATOM	194 O MET	24	36.688 23.054 19.083 1.00 39.75
	MOTA	195 N GLU	25	37.409 21.017 18.469 1.00 41.04
_	MOTA	196 CA GLU	25	38.808 21.397 18.529 1.00 41.50
5	ATOM	197 CB GLU	25	39.685 20.172 18.242 1.00 45.13
	MOTA	198 CG GLU	25	39.356 18.989 19.165 1.00 50.86
	ATOM	199 CD GLU	25	40.586 18.370 19.829 1.00 55.72
	ATOM	200 OE1 GLU	25	41.444 19.126 20.344 1.00 56.58
10	ATOM	201 OE2 GLU	25	40.686 17.122 19.851 1.00 57.47
10	ATOM	202 C GLU	25	39.103 22.536 17.553 1.00 40.38
	ATOM	203 O GLU	25	39.708 23.538 17.928 1.00 37.53
	MOTA	204 N GLU	26	38.655 22.390 16.310 1.00 38.80
	ATOM	205 CA GLU	26	38.885 23.415 15.298 1.00 38.72
15	ATOM	206 CB GLU	26	38.353 22.948 13.943 1.00 40.80
10	MOTA	207 CG GLU 208 CD GLU	26	38.837 21.562 13.555 1.00 45.17
	ATOM ATOM	208 CD GLU 209 OE1 GLU	26 26	38.289 21.099 12.225 1.00 47.49
	MOTA	210 OE2 GLU	26	37.059 21.191 12.023 1.00 50.42 39.087 20.633 11.384 1.00 50.96
	ATOM	211 C GLU	26	
20	MOTA	212 O GLU	26	20 746 05 700
	ATOM	213 N LEU	27	== 1111 2100 33,33
	ATOM	214 CA LEU	27	
	ATOM	215 CB LEU	27	1.00 37.01
	ATOM	216 CG LEU	27	
25	ATOM	217 CD1 LEU	27	2,00 30.21
•	ATOM	218 CD2 LEU	27	30 000
	MOTA	219 C LEU	27	33 054 05 540
	ATOM	220 O LEU	. 27	37.145 27.738 17.820 1.00 37.29
••	ATOM	221 N HIS	28	37.610 25.762 18.776 1.00 42.29
30	ATOM	222 CA HIS	28	38.369 26.378 19.852 1.00 45.83
	ATOM	223 CB HIS	28	38.867 25.311 20.834 1.00 49.02
	ATOM .	224 CG HIS	28	37.786 24.745 21.707 1.00 53.69
	ATOM	225 CD2 HIS	28	36.461 25.024 21.782 1.00 54.33
0.5	ATOM	226 ND1 HIS	28	38.025 23.775 22.660 1.00 54.53
35	ATOM	227 CE1 HIS	28	36.896 23.484 23.283 1.00 53.92
	ATOM	228 NE2 HIS	28	35.932 24.228 22.770 1.00 54.66
	MOTA	229 C HIS	28	39.533 27.202 19.306 1.00 46.70
	MOTA	230 O HIS	28	39.809 28.292 19.806 1.00 46.07
40	ATOM	231 N GLN	29	40.206 26.695 18.277 1.00 47.88
<b>4</b> 0	ATOM	232 CA GLN	29	41.321 27.432 17.686 1.00 49.79
	MOTA	233 CB GLN	29	42.205 26.504 16.841 1.00 51.23
	ATOM	234 CG GLN	29	43.142 25.629 17.673 1.00 55.35
	MOTA	235 CD GLN	29	42.632 24.210 17.843 1.00 57.34
45	ATOM	236 OE1 GLN	29	42.896 23.556 18.856 1.00 58.45
40	ATOM ATOM	237 NE2 GLN	29	41.913 23.717 16.839 1.00 58.43
	ATOM	238 C GLN 239 O GLN	29	40.842 28.609 16.835 1.00 49.61
	ATOM	239 O GLN 240 N LEU	29	41.532 29.621 16.725 1.00 50.02
	ATOM	241 CA LEU	30 30	39.659 28.472 16.245 1.00 49.60 39.081 29.519 15.404 1.00 51 37
50	ATOM	242 CB LEU	30	
	ATOM	243 CG LEU	30	20 21-
)	ATOM	244 CD1 LEU	30	22 22
	ATOM	245 CD2 LEU	. 30	37.770 27.391 12.407 1.00 51.55 39.491 29.212 12.275 1.00 52.87
	ATOM	246 C LEU	30	38.266 30.493 16.233 1.00 52.89
55	ATOM	247 O LEU	30	37.645 31.409 15.694 1.00 53.39
	MOTA	248 N ALA	31	38.271 30.283 17.544 1.00 54.40
	MOTA	249 CA ALA	31	37.509 31.107 18.474 1.00 54.90
	ATOM	250 CB ALA	31	37.875 30.728 19.902 1.00 55.70
<b>60</b>	ATOM	251 C ALA	31	37.674 32.608 18.284 1.00 54.89
60	ATOM	252 O ALA	31	36.695 33.339 18.109 1.00 52.72
	ATOM	253 N TRP	32	38.925 33.055 18.324 1.00 56.51
	MOTA	254 CA TRP	32	39.254 34.468 18.197 1.00 57.22
	MOTA	255 CB TRP	32	40.362 34.816 19.192 1.00 59.36
65	ATOM	256 CG TRP	32	39.979 34.430 20.581 1.00 62.16
65	ATOM	257 CD2 TRP	32	39.717 35.315 21.678 1.00 63.50
	ATOM	258 CE2 TRP	32	39.268 34.519 22.757 1.00 64.21
	ATOM	259 CE3 TRP	32	39.814 36.702 21.855 1.00 63.45
	ATOM	260 CD1 TRP	32	39.697 33.168 21.031 1.00 62.50
70	MOTA	261 NE1 TRP	32	39.265 33.215 22.335 1.00 63.94
70	ATOM	262 CZ2 TRP	32	38.913 35.068 23.995 1.00 63.81
	ATOM	263 CZ3 TRP	32	39.461 37.244 23.087 1.00 62.65
	ATOM	264 CH2 TRP	32	39.016 36.426 24.137 1.00 62.53
	ATOM	265 C TRP	32	39.667 34.850 16.787 1.00 57.28
<i>7</i> 5	MOTA	266 O TRP	32	40.826 35.187 16.526 1.00 58.45
13	ATOM	267 N GLN	33	38.701 34.802 15.879 1.00 54.65
	ATOM	268 CA GLN	.33	38.954 35.145 14.494 1.00 52.60
	ATOM	269 CB GLN	33	39.326 33.892 13.697 1.00 54.99
	ATOM	270 CG GLN	33	40.753 33.411 13.884 1.00 59.00
80	ATOM	271 CD GLN	33	41.772 34.297 13.184 1.00 61.62
00	ATOM ATOM	272 OE1 GLN	33	42.960 33.978 13.148 1.00 63.64
	ATOM	273 NE2 GLN	33	41.312 35.415 12.624 1.00 63.55

•	ATOM	274	С	GLN	33	37.737	35.801	13.863	1.00 49.63
	ATOM ATOM	275 276	о И	GLN THR	33 34	36.785 37.763	35.124 37.125	13.489	1.00 47.22
_	MOTA	277	CA	THR	34	36.678	37.863	13.771 13.139	1.00 47.47 1.00 45.87
5	MOTA	278	СВ	THR	34	36.159	39.019	14.033	1.00 46.83
	ATOM ATOM	279 280	OG1 CG2		34 34	·37.237 35.556	39.911 38.475	14.346	1.00 46.09
	MOTA	281	C	THR	34	37.269	38.446	15.321 11.856	1.00 47.41
10	ATOM	282	0	THR	34	38.469	38.731	11.797	1.00 44.57
10	MOTA	283	N	HIS	35	36.451	38.605	10.822	1.00 41.42
	ATOM ATOM	284 285	CA CB	HIS HIS	35 35	36.964 35.894	39.168 39.157	9.581 8.487	1.00 37.99 1.00 34.94
	MOTA	286	CG	HIS	35	. 35.570	37.792	7.967	1.00 34.34
15	ATOM	287		HIS	35	36.167	37.037	7.015	1.00 30.88
10	MOTA MOTA	288 289		HIS HIS	35 35	34.510 34.467	37.047 35.893	8.438 7.797	1.00 31.87 1.00 30.43
	MOTA	290		HIS	35	35.463	35.862	6.929	1.00 30.43
	MOTA	291	C	HIS	35	37.414	40.601	9.844	1.00 36.88
20	ATOM ATOM	292 293	O N	HIS THR	35 36	36.856 38.439	41.287 41.042	10.697 9.124	1.00 35.24
	ATOM	294	CA	THR	36	38.949	42.402	9.276	1.00 38.20 1.00 39.26
	MOTA	295	CB	THR	36	40.319	42.550	8.597	1.00 39.89
	ATOM ATOM	296 297	0G1	THR THR	36 36	40.181 41.312	42.304 41.548	7.192	1.00 40.21
25	MOTA	298	C	THR	36	37.959	43.346	9.178 8.599	1.00 40.05 1.00 39.52
	MOTA	299	0	THR	36	37.070	42.894	7.873	1.00 38.71
	ATOM ATOM	300 301	N CA	TYR TYR	37 37	38.101 37.186	44.648	8.824	1.00 40.48
	ATOM	302	CB	TYR	37	37.474	45.595 47.026	8.197 8.653	1.00 41.59 1.00 44.12
30	ATOM	303	CG	TYR	37	37.124	47.289	10.099	1.00 46.75
	ATOM ATOM	304 305	CD1	TYR	37 37	38.080	47.149	11.110	1.00 48.09
	ATOM	306		TYR TYR	37 37	37.754 35.831	47.392 47.675	12.453 10.460	1.00 49.23 1.00 47.60
25	ATOM	307	CE2	TYR	37	35.493	47.916	11.795	1.00 49.16
35	ATOM ATOM	308 309	CZ	TYR	37 27	36.456	47.775	12.786	1.00 49.69
	ATOM	310	OН С	TYR TYR	37 37	36.120 37.269	48.027 45.515	14.100 6.678	1.00 48.49 1.00 41.21
	ATOM	311	0	TYR	37	36.265	45.673	5.988	1.00 39.83
40	ATOM ATOM	312 313	N CA	GLU	38	38.469	45.270	6.158	1.00 40.73
10	ATOM	314	CB	GLU GLU	38 38	38.652 40.136	45.161 45.020	4.715 4.358	1.00 41.99 1.00 43.80
	ATOM	315	CG	GLU	38	40.985	46.242	4.668	1.00 46.95
	ATOM ATOM	316 317	CD	GLU	38	41.266	46.412	6.154	1.00 48.29
45	ATOM	318		GLU GLU	38 38	41.815 40.948	47.470 45.493	6.528 6.943	1.00 50.72 1.00 48.78
	ATOM	319	С	GLU	38	37.896	43.949	4.185	1.00 41.21
	ATOM ATOM	320 321	O N	GLU	38	37.284	44.000	3.122	1.00 39.46
	ATOM	322	CA	GTA GTA	39 39	37.946 37.265	42.854 41.632	4.935 4.527	1.00 41.37 1.00 41.22
50	MOTA	323	СВ	GLU	39	37.693	40.473	5.429	1.00 42.06
	ATOM ATOM	324 325	CG CD	GLU	39	39.208	40.289	5.453	1.00 46.35
	ATOM	325		GLU GLU	39 39	39.668 39.234	39.164 39.126	6.363 7.534	1.00 48.63 1.00 48.96
<b>E E</b>	ATOM	327	OE2	GLU	39	40.476	38.324	5.909	1.00 50.59
55	MOTA MOTA	328	c o	GLU	39	35.756	41.844	4.581	1.00 39.62
	ATOM	329 330	N	GLU ILE	39 40	35.023 35.296	41.339 42.601	3.728 5.575	1.00 40.20 1.00 37.13
	ATOM	331	CA	ILE	40	33.873	42.885	5.706	1.00 36.49
60	ATOM ATOM	332 333	CB	ILE	40	33.541	43.587	7.058	1.00 35.15
	ATOM	334	CG2 CG1		40 40	32.105 33.715	44.100 42.603	7.054 8.219	1.00 34.00 1.00 34.57
	ATOM	335	CD1	ILE	40	32.853	41.351	8.102	1.00 32.97
	MOTA	336	C	ILE .	40	33.445	43.784	4.557	1.00 36.47
65	MOTA MOTA	337 338	O N	ILE Lys	40 41	32.386 34.277	43.582 44.772	3.966 4.233	1.00 35.95 1.00 37.54
	MOTA	339	CA	LYS	41	33.955	45.688	3.141	1.00 37.34
	ATOM	340	CB	LYS	41	35.023	46.774	3.002	1.00 41.50
	ATOM ATOM	341 342	CG CD	LYS LYS	41 41	34.532 33.917	48.021 49.022	2.277 3.257	1.00 45.40
70	ATOM	343	CE	LYS	41	32.816	48.394	4.110	1.00 49.51 1.00 50.14
	MOTA	344	NZ	LYS	41	32.365	49.280	5.217	1.00 51.19
	ATOM ATOM	345 346	С 0	LYS LYS	41 41	33.876 32.987	44.899 45.121	1.846 1.023	1.00 36.39
<b>-</b> 7	ATOM	347	N	ALA	42	34.813	43.121	1.679	1.00 34.38 1.00 35.77
75	ATOM	348	CA	ALA	42	34.855	43.134	0.492	1.00 36.18
	ATOM ATOM	349 350	CB C	ALA ALA	42 42	35.999 33.523	42.132 42.409	0.599	1.00 37.07
	ATOM	351	o	ALA	42	32.958	42.409	0.345 -0.749	1.00 35.76 1.00 35.23
80	ATOM	352	N	TYR	43	33.015	41.868	1.451	1.00 34.54
30	ATOM ATOM	353 354	CA CB	TYR TYR	43 43	31.740 31.423	41.155 40.539	1.423 2.794	1.00 33.59 1.00 33.00
								~.,,,,	00 33.00

	ATOM	355 CG TYR	43	22 176			
				32.175			
****	ATOM	356 CD1 TYR	43	32.035	38.138	2.275	1.00 31.79
	ATOM	357 CE1 TYR	43	32.734	36.959		
_	ATOM	358 CD2 TYR	43	33.031			
5	ATOM	359 CE2 TYR	43.				
•		4 - 1		33.735			1.00 32.13
	MOTA	360 CZ TYR	43	33.583	36.902	3.643	1.00 32.91
	MOTA	361 OH TYR	43	34.287	35.750	3.922	1.00 32.24
	MOTA (	362 C TYR	43	30.589			
	ATOM					1.017	1.00 33.94
10			43	29.697		0.277	1.00 33.69
10	ATOM	364 N GLN	44	30.605	43.295	1.510	1.00 34.41
	MOTA	365 CA GLN	44	29.540		1.206	
	MOTA	366 CB GLN	44				1.00 35.55
				29.571		2.210	1.00 36.41
	ATOM	367 CG GLN	44	29.489		3.665	1.00 38.05
a	MOTA	368 CD GLN	44	29.509	46.090	4.667	1.00 39.51
15	ATOM	369 OE1 GLN	44	30.353			
	ATOM					4.592	1.00 40.40
			44	28.588	46.056	5.621	1.00 38.09
	ATOM	371 C GLN	44	29.635	44.774	-0.220	1.00 35.22
	ATOM	372 O GLN	44	28.657	45.279	-0.769	
	ATOM	373 N SER					1.00 35.57
20		_	45	30.813	44.645	-0.821	1.00 36.36
20	ATOM	374 CA SER	45	31.029	45.115	-2.186	1.00 37.51
	ATOM	375 CB SER	45	32.490	45.520	-2.385	
	ATOM	376 OG SER	45				1.00 36.45
				32.830	46.585	-1.519	1.00 37.77
	ATOM	377 C SER	45	30.649	44.065	-3.224	1.00 37.52
0.5	ATOM	378 O SER	45	30.433	44.390	-4.394	1.00 37.81
25	ATOM	379 N LYS	46	30.581	42.805		
	ATOM					-2.804	1.00 37.01
			46	30.207	41.729	-3.718	1.00 37.49
	MOTA	381 CB LYS	46	30.185	40.385	-2.978	1.00 38.89
	ATOM	382 CG LYS	46	31.554	39.830	-2.619	
	ATOM						1.00 41.39
30			46	32.285	39.347	-3.859	1.00 43.62
50	ATOM	384 CE LYS	46	33.618	38.716	-3.501	1.00 45.39
	ATOM	385 NZ LYS	46	33.460	37.587	-2.542	1.00 46.78
	ATOM	386 C LYS	46	28.811			
					42.027	-4.261	1.00 36.47
	ATOM	387 O LYS	46	28.024	42.714	-3.616	1.00 34.79
0.5	ATOM	388 N SER	47	28.505	41.526	-5.450	1.00 35.94
35	MOTA	389 CA SER	47	27.181	41.741	-6.011	
	ATOM						1.00 36.64
			47	27.149	41.341	-7.486	1.00 36.69
	ATOM	391 OG SER	47	27.443	39.964	-7.636	1.00 35.57
	ATOM	392 C SER	47	26.232	40.843	-5.225	1.00 37.24
	ATOM	393 O SER	47	26.672			
40	ATOM				39.994	-4.452	1.00 36.62
10		394 N ARG	48	24.934	41.026	~5.419	1.00 37.93
	ATOM	395 CA ARG	48	23.957	40.202	-4.726	1.00 37.32
	ATOM	396 CB ARG	48	22.551	40.762		
	ATOM	- ·				-4.966	1.00 38.56
			48	21.427	39.977	-4.315	1.00 38.73
45	ATOM	398 CD ARG	48	20.311	40.908	-3.869	1.00 39.69
45	ATOM	399 NE ARG	48	19.091	40.181	-3.530	
	ATOM	400 CZ ARG	48	18.294			1.00 41.75
					39.611	-4.429	1.00 43.27
	ATOM	401 NH1 ARG	48	18.588	39.688	-5.721	1.00 43.91
	ATOM	402 NH2 ARG	48	17.203	38.965	-4.041	1.00 41.76
	ATOM	403 C ARG	48	24.073	38.754	-5.220	_
50	ATOM	404 O ARG	48				1.00 36.87
				23.928	37.806	-4.441	1.00 35.81
	MOTA	405 N GLU	49	24.352	38.592	-6.511	1.00 34.76
	ATOM	406 CA GLU	49	24.501	37.268	-7.113	
	ATOM	407 CB GLU	49	24.643			1.00 35.71
	ATOM				37.371	-8.636	1.00 38.45
55		408 CG GLU	49	23.676	38.328	-9.302	1.00 44.94
33	ATOM	409 CD GLU	49	24.015	39.782	-9.028	1.00 47.01
	ATOM	410 OE1 GLU	49	25.099	40.231		
	ATOM					-9.460	1.00 49.86
			49	23.201	40.476	-8.380	1.00 46.92
	ATOM	412 C GLU	49	25.751	36.591	-6.568	1.00 33.86
	ATOM	413 O GLU	49	25.731	35.414	-6.213	1.00 33.86
60	ATOM	414 N ALA	50	26.843	37.344		
	ATOM					-6.511	1.00 32.28
		415 CA ALA	50	28.098	36.804	-6.021	1.00 31.98
	ATOM	416 CB ALA	50	29.206	37.849	-6.139	1.00 30.17
	ATOM	417 C ALA	50	27.975	36.322		
	ATOM					-4.579	1.00 31.48
65			50	28.373	35.201	-4.263	1.00 29.44
03	ATOM	419 N LEU	51	27.422	37.159	~3.703	1.00 30.98
	ATOM	420 CA LEU	51	27.289	36.762		
	ATOM					-2.305	1.00 30.66
			51	26.830	37.940	-1.441	1.00 30.32
	ATOM	422 CG LEU	51	26.893	37.675	0.070	1.00 32.08
	ATOM	423 CD1 LEU	51	28.267	37.144	0.444	
70	MOTA	424 CD2 LEU	51				1.00 32.44
				26.594	38.952	0.842	1.00 32.02
	ATOM	425 C LEU	51	26.332	35.582	-2.156	1.00 29.32
	MOTA	426 O LEU	51	26.601	34.652	-1.393	1.00 28.16
	ATOM	427 N TRP	52	25.220	35.614		
						-2.886	1.00 28.73
75	ATOM	428 CA TRP	52	24.261	34.520	-2.835	1.00 28.59
<i>7</i> 5	MOTA	429 CB TRP	52	23.076	34.781	-3.770	1.00 30.93
	ATOM	430 CG TRP	52	21.878	35.296	-3.050	
	MOTA	431 CD2 TRP					1.00 35.78
			52	20.905	34.513	-2.351	1.00 39.02
	MOTA	432 CE2 TRP	52	19.99ሕ	35.413	-1.759	1.00 39.44
00	ATOM	433 CE3 TRP	52	20.720	33.135	-2.161.	1.00 40.28
80	ATOM	434 CD1 TRP	52	21.524			
	ATOM				36.602	-2.865	1.00 35.55
	AI ON	435 NE1 TRP	52	20.391	36.681	-2.089	1.00 38.68

								•	•
	ATOM	436	CZ	2 TRP	52	18.905	34.980	-0.991	1.00 42.34
	ATOM	437	CZ:	3 TRP	52	19.644	32.705	-1.398	1.00 41.70
	MOTA	438	CH		52	18.749	33.626	-0.821	1.00 42.77
	MOTA	439	С	TRP	52	24.929	33.213	-3.231	1.00 27.04
5	ATOM	440	0	TRP	52	24.704	32.182	-2.609	1.00 26.75
	ATOM	441	N	GLN	53	25.742	33.259	-4.279	1.00 26.75
	ATOM	442	CA	GLN	53	26.446	32.071	-4.740	1.00 27.50
	ATOM	443	СВ	GLN	53	27.209	32.391	-6.031	1.00 31.81
	ATOM	444	CG	GLN	53	27.894	31.198	-6.678	1.00 36.92
10	MOTA	445	CD	GLN	53	28.277	31.456	-8.137	1.00 42.85
	ATOM	446	OE!		53 .	28.893	30.609	-8.786	1.00 42.85
	ATOM	447	NE		53	27.904	32.628	-8.657	1.00 43.92
	ATOM	448	c	GLN	53	27.403	31.558	-3.655	
	ATOM	449	ŏ	GLN	53	27.530	30.354	-3.449	1.00 26.49
15	ATOM	450	N	GLN	54	28.071	32.473	-2.960	1.00 24.81
	ATOM	451	CA	GLN	54	28.992	32.094	-1.890	1.00 25.88
	ATOM	452	CB	GLN	54	29.727	33.323		1.00 27.32
	ATOM	453	CG	GLN	54	30.846		-1.343	1.00 31.35
	MOTA	454	CD	GLN	54		33.861	-2.229	1.00 37.27
20	ATOM	455		GLN	54	31.493	35.112	-1.645	1.00 41.33
20		456	NE2		54	31.105	36.239	-1.969	1.00 44.63
	ATOM					32.474	34.916	-0.766	1.00 40.57
	ATOM ATOM	457 458	C	GLN	54 54	28.210	31.445	-0.754	1.00 26.99
	ATOM		0	GLN	54	28.621	30.423	-0.201	1.00 25.42
25		459	N	CYS	55	27.084	32.060	-0.402	1.00 26.01
20	MOTA	460	CA	CYS	55	26.236	31.550	0.663	1.00 25.09
	ATOM	461	CB	CYS	55	25.097	32.536	0.935	1.00 26.44
	ATOM	462	SG	CYS	55	25.637	34.013	1.827	1.00 26.26
	MOTA	463	C	CYS	55	25.673	30.175		1.00 24.90
30	ATOM	464	0	CYS	55	25.603	29.284	1.151	1.00 23.90
30	ATOM	465	N	ALA	56	25.287	30.011	-0.958	1.00 22.85
	ATOM	466	CA	ALA	56	24.733	28.752	-1.438	1.00 22.57
	ATOM	467	CB	ALA	56	24.310	28.903	-2.878	1.00 18.31
	ATOM	468	C	ALA	56	25.765	27.625	-1.305	1.00 23.49
35	MOTA	469	0	ALA	56	25.425	26.499	-0.967	1.00 24.70
, 33	MOTA	470	N	ILE	57	27.027	27.937	-1.575	1.00 24.87
	ATOM	471	CA	ILE	57	28.094	26.945	-1.471	1.00 26.21
	MOTA	472	СВ	ILE	57	29.390	27.479	-2.104	1.00 27.82
	MOTA	473	CG2		57	30.597	26.671	-1.616	1.00 29.94
40	ATOM	474	CG1		57	29.260	27.432	-3.630	1.00 28.92
<b>4</b> 0	MOTA	475		ILE	57	30.484	27.913	-4.374	1.00 31.67
	MOTA	476	С	ILE	57	28.348	26.554	-0.012	1.00 27.09
	ATOM	477	0	ILE	57	28.465	25.370	0.306	1.00 27.29
	MOTA	478	N	GLN	58	28.416	27.547	0.872	1.00 26.96
45	MOTA	479	CA	GLN	58	28.637	27.289	2.291	1.00 28.94
45	MOTA	480	CB	GLN	58	28.761	28.613	3.056	1.00 31.47
	ATOM	481	CG	GLN	58	28.855	28.471	4.571	1.00 37.58
	ATOM	482	CD	GLN	58	29.890	27.439	5.012	1.00 43.52
	ATOM	483	OE1	GLN	58	31.043	27.458	4.557	1.00 45.14
<b>-</b> 0	ATOM	484	NE2	GLN	58	29.482	26.536	5.907	1.00 40.77
50	MOTA	485	С	GLN	58	27.495	26.449	2.866	1.00 25.89
	ATOM	486	0	GLN	58	27.725	25.506	3.619	1.00 25.53
	ATOM	487	N	ILE	59	26.264	26.794	2.511	1.00 24.98
	ATOM	488	CA	ILE	· 59	25.104	26.049	2.985	1.00 22.92
	ATOM	489	CB	ILE	59	23.787	26.717	2.531	1.00 23.63
55	ATOM	490	CG2	ILE	59	22.617	25.752	2.715	1.00 21.17
	ATOM	491	CG1	ILE	59	23.570	28.021	3.307	
	ATOM	492	CD1	ILE	59	22.311	28.781	2.879	1.00 23.75
	ATOM	493	С	ILE	59	25.133	24.618	2.448	1.00 23.06
	ATOM	494	0	ILE	59	24.867	23.668	3.181	1.00 21.94
60	ATOM	495	N	THR	60	25.445	24.470	1.163	1.00 23.15
	MOTA	496	CA	THR	60	25.510	23.149	0.552	1.00 23.13
	ATOM	497	СВ	THR	60	25.837	23.243	-0.956	1.00 22.65
	ATOM	498		THR	60	24.787	23.946	-1.631	
•	ATOM	499	CG2		60	25.986	21.854	-1.562	1.00 24.06
65	ATOM	500	c	THR	60	26.596	22.333		1.00 22.93
	ATOM	501	ō	THR	60	26.423	21.148	1.244	1.00 22.48
	ATOM	502	N	HIS	61	27.715	22.984	1.514	1.00 24.18
	ATOM	503	CA	HIS	61	28.837	22.324	1.537	1.00 23.04
	ATOM	504	CB	HIS	61			2.194	1.00 22.43
70	ATOM	505	CG	HIS	61	29.958	23.346	2.401	1.00 23.21
. •	ATOM	506				31.257	22.753	2.846	1.00 26.52
	ATOM	507		HIS	61 61	32.298	23.298	3.520	1.00 28.76
	ATOM			HIS	61	31.623	21.455	2.566	1.00 28.62
		508		HIS	61	32.830	21.224	3.049	1.00 27.83
<i>7</i> 5	ATOM	509		HIS	61	33.263	22.326	3.634	1.00 29.16
, 5	ATOM	510	C.	HIS	61	28.356	21.753	3.528	1.00 22.71
	ATOM	511	0	HIS	61	28.583	20.582	3.837	1.00 22.54
	ATOM	512	N	ALA	62	27.659	22.579	4.297	1.00 21.43
	ATOM	513	CA	ALA	62	27.141	22.168	5.596	1.00 22.12
80	ATOM	514	CB	ALA	62	26.597	23.392	6.349	1.00 17.66
JU	ATOM	515	C	ALA	62	26.059	21.088	5.480	1.00 21.21
	ATOM	516	0	ALA	62	25.959	20.208	6.340	1.00 22.10

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	MOTA	517 N ILE	63	25.24	21.157	4.428	1.00 21.36
	ATOM	518 CA ILE	63	24.185 2	20.172		1.00 21.14
	ATOM ATOM	519 CB ILE 520 CG2 ILE	63 63		20.582	3.075	1.00 20.43
5	ATOM	521 CG1 ILE	63		19.429 21.795	2.711 3.493	1.00 20.13
	MOTA	522 CD1 ILE	63		22.260	2.425	1.00 20.25 1.00 22.13
	MOTA	523 C ILE	63		18.804	3.901	1.00 22.13
	ATOM	524 O ILE	63		17.779	4.323	1.00 22.39
10	ATOM ATOM	525 N GLN 526 CA GLN	64 64	25.875 1	18.787	3.155	1.00 22.82
20	ATOM	527 CB GLN	64		17.528 17.782	2.801 1.846	1.00 22.75
	MOTA	528 CG GLN	64	27.200 1	18.212	0.465	1.00 21.87 1.00 24.19
	ATOM	529 CD GLN	64	28.293 1	18.402	-0.582	1.00 26.74
15	ATOM ATOM	530 OE1 GLN 531 NE2 GLN	64		8.432	-1.783	1.00 29.29
10	MOTA	531 NE2 GLN 532 C GLN	64 64		18.541 16.798	-0.140	1.00 22.66
	MOTA	533 O GLN	64		5.575	4.064 4.139	1.00 22.10 1.00 21.93
	ATOM	534 N TYR	65		7.554	5.064	1.00 21.93
20	MOTA	535 CA TYR	65		6.964	6.335	1.00 23.86
20	ATOM ATOM	536 CB TYR 537 CG TYR	65		7.980	7.171	1.00 26.62
	ATOM	537 CG TYR 538 CD1 TYR	65 65		8.030	6.823	1.00 30.04
	ATOM	539 CE1 TYR	65		6.986	7.140 6.807	1.00 32.17 1.00 33.14
25	ATOM	540 CD2 TYR	65		9.128	6.160	1.00 30.53
25	MOTA	541 CE2 TYR	65		9.161	5.818	1.00 33.67
	ATOM ATOM	542 CZ TYR 543 OH TYR	65 · 65		8.086	6.147	1.00 36.28
	ATOM	544 C TYR	65		B.109 6.449	5.821	1.00 40.50
00	ATOM	545 O TYR	65		5.498	7.120	1.00 22.30 1.00 23.33
30	MOTA	546 N VAL	66		7.071	6.938	1.00 20.36
	ATOM	547 CA VAL	66		6.598	7.637	1.00 20.83
	MOTA MOTA	548 CB VAL 549 CG1 VAL	66		7.574	7.502	1.00 18.86
	ATOM	549 CG1 VAL 550 CG2 VAL	66 66		6.965	8.176	1.00 19.22
35	ATOM	551 C VAL	66		8.914 5.246	8.159 7.040	1.00 16.99 1.00 20.81
	ATOM	552 O VAL	66		4.370	7.740	1.00 20.81
	ATOM	553 N VAL	67	24.048 1	5.085	5.739	1.00 22.31
	ATOM ATOM	554 CA VAL 555 CB VAL	67 67		3.830	5.062	1.00 21.44
40	ATOM	555 CB VAL 556 CG1 VAL	67 67		3.943 2.593	3.544	1.00 22.66
	ATOM	557 CG2 VAL	67		4.992	2.872 2.939	1.00 22.40 1.00 23.72
	MOTA	558 C VAL	67		2.726	5.653	1.00 23.72
	ATOM	559 O VAL	67		1.616	5.913	1.00 22.69
45	ATOM ATOM	560 N GLU 561 CA GLU	68		3.040	5.879	1.00 23.93
10	ATOM	561 CA GLU 562 CB GLU	68 68		2.072 2.652	6.463	1.00 25.73
	ATOM	563 CG GLU	68		2.972	6.483 5.097	1.00 31.22 1.00 35.81
	ATOM	564 CD GLU	68	29.333 11	1.745	4.375	1.00 42.48
50	ATOM	565 OE1 GLU	68		0.692	4.362	1.00 42.24
50	ATOM ATOM	566 OE2 GLU 567 C GLU	68 68		1.841	3.808	1.00 45.88
	ATOM	568 O GLU	68		1.749 0.597	7.882 8.322	1.00 25.40
	ATOM	569 N PHE	69		2.776	8.590	1.00 23.68 1.00 23.61
55	ATOM	570 CA PHE	69	25.386 12	2.633	9.956	1.00 22.83
55	ATOM	571 CB PHE	69		.001	10.448	1.00 21.69
	ATOM ATOM	572 CG PHE 573 CD1 PHE	69 69		3.989 3.412	11.822	1.00 24.10
	ATOM	574 CD2 PHE	69		1.613	12.912 12.034	1.00 21.29 1.00 23.32
60	MOTA	575 CE1 PHE	69		3.459	14.184	1.00 23.32
60	ATOM	576 CE2 PHE	69	22.444 14	1.667	13.308	1.00 20.43
	ATOM	577 CZ PHE 578 C PHE	69		1.089	14.386	1.00 22.91
	MOTA MOTA	578 C PHE 579 O PHE	69 69		.598	9.967	1.00 23.85
	MOTA	580 N ALA	70		0.659 1.757	10.764	1.00 25.22
65	ATOM	581 CA ALA	70		.851	9.058 8.962	1.00 23.28 1.00 22.31
	ATOM	582 CB ALA	70		.382	7.926	1.00 22.02
	ATOM	583 C ALA	70		.406	8.618	1.00 22.95
	MOTA MOTA	584 O ALA 585 N LYS	70		. 457	9.205	1.00 21.88
70	ATOM	585 N LYS 586 CA LYS	71 71		.241	7.664	1.00 23.24
	ATOM	587 CB LYS	71		.911	7.249 6.065	1.00 26.69
	ATOM	588 CG LYS	71		.701	4.848	1.00 27.02 1.00 28.09
	ATOM	589 CD LYS	71	25.300 9	.022	3.802	1.00 28.09
75	ATOM	590 CE LYS	71	25.970 7	.770	3.257	1.00 30.06
13	ATOM ATOM	591 NZ LYS	71		.147	2.221	1.00 33.92
	ATOM	592 C LYS 593 O LYS	71 71		.114	8.379	1.00 26.63
	ATOM	594 N ARG	72		.880	8.370 9.347	1.00 26.95
00	ATOM	595 CA ARG	72		.120	10.449	1.00 24.99 1.00 27.31
80	ATOM	596 CB ARG	72	27.051 7	.892	10.880	1.00 28.59
	ATOM	597 CG ARG	72	28.031 8	.064	9.732	1.00 29.69

	ATOM	598	CD	ARG	72 ·	29.365	0 502	10 100	1 00 21 02
							8.593	10.180	1.00 31.03
	ATOM	599	NE	ARG	72	30.268	8.732	9.044	1.00 33.59
	ATOM	600	CZ	ARG	72	31.546	9.081	9.145	1.00 38.36
	ATOM	601	NH1		72				
5						32.076	9.326	10.338	1.00 39.73
9	ATOM	602	NH2	ARG	72	32.291	9.194	8.054	1.00 39.15
	MOTA	603	С	ARG	72	24.891	6.874	11.643	1.00 27.40
	MOTA	604	0	ARG	72	25.333			
							6.367	12.675	1.00 29.05
	MOTA	605	N	ILE	73	23.618	7.243	11.504	1.00 26.22
_	MOTA	606	CA	ILE	73	22.64B	7.015	12.566	
10									
10	MOTA	607	СВ	ILE	73	21.631	8.178	12.705	1.00 22.57
	MOTA	608	CG2	ILE	73	20.568	7.810	13.744	1.00 23.16
	MOTA	609	CG1	ILE	73	22.352	9.463	13.124	
									1.00 23.44
	ATOM	610	CD1	ILE	73	21.412	10.645	13.411	1.00 23.02
	ATOM	611	С	ILE	73	21.884	5.747	12.205	1.00 25.40
15	ATOM	612	0	ILE	73	21.067	5.737	11.276	
10									1.00 23.63
	MOTA	613	N	THR	74	22.155	4.679	12.947	1.00 25.29
	ATOM	614	CA	THR	74	21.521	3.388	12.712	1.00 27.03
	MOTA	615	СВ	THR	74				
						21.790	2.433	13.878	1.00 29.63
00	ATOM	616	0G1	THR	74	23.157	2.555	14.286	1.00 33.21
20	ATOM	617	CG2	THR	74	21.531	0.998	13.445	1.00 33.49
	ATOM								
		618	C	THR	74	20.007	3.466	12.510	1.00 25.59
	ATOM	619	0	THR	74	19.479	2.985	11.508	1.00 25.68
	ATOM	620	N	GLY	75	19.315	4.063	13.472	
	ATOM								1.00 26.41
25		621	CA	GLY	75	17.868	4.181	13.388	1.00 25.95
25	ATOM	622	С	GLY	75	17.382	4.896	12.139	1.00 25.86
	MOTA	623	0	GLY	75	16.324	4.563		
								11.603	1.00 25.03
	MOTA	624	N	PHE	76	18.146	5.877	11.667	1.00 24.84
	ATOM	625	CA	PHE	76	17.752	6.612	10.466	1.00 25.41
	ATOM	626	СВ	PHE	76	18.643			
30							7.847	10.259	1.00 23.08
30	MOTA	627	CG	PHE	76	18.319	8.634	9.005	1.00 25.15
	ATOM	628	CD1	PHE	76	18.889	8.291	7.778	1.00 25.38
	ATOM	629	CD2						
					76	17.443	9.714	9.050	1.00 23.74
	MOTA	630	CEl	PHE	76	18.592	9.015	6.621	1.00 25.08
_	MOTA	631	CE2	PHE	76	17.140	10.445	7.891	1.00 24.62
35	ATOM								
55		632	CZ	PHE	76	17.717	10.092	6.680	1.00 22.76
	ATOM	633	С	PHE	76	17.828	5.717	9.240	1.00 24.88
	ATOM	634	0	PHE	76	16.888	5.665	8.447	
	MOTA								1.00 24.05
		635	N	MET	77	18.943	5.007	9.088	1.00 25.71
40	ATOM	636	CA	MET	<b>7</b> 7	19.123	4.136	7.937	1.00 26.70
40	MOTA	637	СВ	MET	77	20.575	3.655	7.852	
									1.00 28.75
	ATOM	638	CG	MET	77	21.577	4.773	7.554	1.00 30.31
	MOTA	639	SD	MET	77	21.118	5.827	6.136	1.00 31.94
	ATOM	640	CE	MET	77				
						21.818	4.891	4.717	1.00 35.36
4 =	MOTA	641	С	MET	77	18.164	2.947	7.920	1.00 28.58
45	MOTA	642	0	MET	77	18.071	2.233	6.919	1.00 28.47
	MOTA	643	N	GLU	78				
						17.449	2.737	9.022	1.00 29.72
	ATOM	644	CA	GLU	78	16.477	1.652	9.091	1.00 30.71
	ATOM	645	CB	GLU	78	16.312	1.153	10.525	1.00 32.46
	ATOM	646							
50			CG	GLU	78	17.393	0.187	10.966	1.00 38.31
50	ATOM	647	CD	GLU	78	17.235	-0.231	12.411	1.00 40.71
	MOTA	648	OEL	GLU	78	16.118	-0.633		
								12.794	1.00 43.62
	MOTA	649	OE2	GLU	78	18.226	-0.160	13.163	1.00 43.48
	ATOM	650	С	GLU	78	15.129	2.121	8.558	1.00 31.42
	ATOM	651	Ó	GLU	78	14.226			
55							1.315	8.336	1.00 29.99
55	MOTA	652	N	LEU	79	14.984	3.428	8.368	1.00 30.08
	ATOM	653	CA	LEU	79	13.735	3.958	7.832	1.00 29.88
	ATOM	654	СВ	LEU	79	13.658			
							5.476	8.044	1.00 25.4
	ATOM	655	CG	LEU	79	13.653	5.967	9.495	1.00 25.48
	ATOM	656	CD1	LEU	79	13.735	7.483	9.516	1.00 23.35
60	ATOM	657		LEU					
00					79	12.392	5.480	10.219	1.00 24.40
	ATOM ·	658	С	LEU	79	13.745	3.633	6.339	1.00 29.03
	ATOM	659	0	LEU	79	14.815	3.562	5.735	
									1.00 26.93
	ATOM	660	N	CYS	80	12.573	3.419	5.744	1.00 30.41
	ATOM	661	CA	CYS	80	12.524	3.114	4.314	1.00 32.22
65	ATOM	662	CB	CYS	80				
00						11.081	2.931	3.830	1.00 33.77
	ATOM	663	SG	CYS	80	10.113	4.443	3.665	1.00 35.11
	MOTA	664	С	CYS	80	13.182	4.281	3.582	1.00 32.79
	ATOM								
		665	0	CYS	80	13.107	5.432	4.032	1.00 31.43
<b>70</b>	MOTA	666	N	GLN	81	13.825	3.986	2.458	1.00 32.81
70	ATOM	667	CA	GLN	81	14.533	5.009		
								1.694	1.00 33.38
	ATOM	668	CB	GLN	81	15.144	4.401	0.433	1.00 36.20
	ATOM	669	CG	GLN	81	15.988	5.382	-0.353	1.00 40.19
	ATOM	670	CD						
				GLN	81	16.894	4.693	-1.346	1.00 42.67
75	MOTA	671	OE1	GLN	81	16.429	4.055	-2.295	1.00 44.22
<i>7</i> 5	MOTA	672	NE2	GLN	81	18.201	4.808	-1.128	1.00 42.74
	ATOM	673							
			C	GLN	81	13.702	6.225	1.317	1.00 32.60
	ATOM	674	0	GLN	81	14.218	7.346	1.286	1.00 31.70
	ATOM	675	N	ASN	82	12.423	6.017	1.019	1.00 30.05
90	ATOM	676	CA	ASN	82	11.571	7.139	0.655	1.00 29.42
80	ATOM	677	CB	ASN	82	10.160	6.665	0.317	1.00 30.85
	ATOM	678	CG	ASN	82	9.211	7.818		
	0.2	3.0		กอเร	<b>52</b>	2.211		0.086	1.00 33.27

				0,		
	ATOM	679 OD1 ASN	82	8.605 8.345	1 026	1 00 25 00
	ATOM	680 ND2 ASN	82	9.091 8.236	1.026 -1.168	1.00 35.99 1.00 34.74
	ATOM	681 C ASN	82	11.508 8.175	1.775	1.00 34.74 1.00 27.40
_	ATOM	682 O ASN	82	11.635 9.372	1.527	1.00 26.11
5	ATOM	683 N ASP	83	11.310 7.716	3.008	1.00 26.77
	MOTA	684 CA ASP	83	11.236 8.635	4.140	1.00 25.04
	ATOM	685 CB ASP	83	10.629 7.921	5.354	1.00 24.28
	ATOM	686 CG ASP	83	9.136 7.649	5.175	1.00 25.67
10	MOTA	687 OD1 ASP	83	8.564 8.116	4.166	1.00 26.27
10	MOTA	688 OD2 ASP	83	8.531 6.978	6.034	1.00 25.59
	MOTA	689 C ASP	83	12.594 9.253	4.471	1.00 23.54
	MOTA	690 O ASP	83	12.663 10.407	4.886	1.00 24.66
	MOTA	691 N GLN	84	13.672 8.497	4.276	1.00 22.13
15	MOTA	692 CA GLN	84	15.008 9.029	4.518	1.00 23.18
15	MOTA	693 CB GLN	84	16.076 8.012	4.118	1.00 22.97
	MOTA	694 CG GLN	84	16.201 6.783	5.019	1.00 24.40
	MOTA	695 CD GLN	84	17.276 5.826	4.511	1.00 23.49
	MOTA	696 OE1 GLN	84	18.170 6.233	3.777	1.00 24.96
20	MOTA	697 NE2 GLN	84	17.202 4.563	4.916	1.00 22.35
20	ATOM	698 C GLN	84	15.176 10.290	3.663	1.00 24.86
	ATOM	699 O GLN	84	15.624 11.331	4.147	1.00 24.41
	MOTA	700 N ILE	85	14.819 10.175	2.384	1.00 24.70
	MOTA ATOM	701 CA ILE 702 CB ILE	85	14.908 11.283	1.433	1.00 24.80
25	ATOM		85	14.426 10.838	0.013	1.00 26.48
20	ATOM		. 85	14.299 12.043	-0.917	1.00 23.15
	ATOM		85	15.410 9.827	-0.588	1.00 26.97
	ATOM		85 85	16.768 10.394	-0.861	1.00 29.45
	ATOM	706 C ILE 707 O ILE	85 85	14.067 12.473	1.905	1.00 24.78
30	ATOM	708 N LEU	85 86	14.539 13.614	1.914	1.00 25.40
00	ATOM	709 CA LEU	86	12.829 12.203	2.310	1.00 23.18
	ATOM	710 CB LEU	86	11.935 13.259	2.784	1.00 22.88
	ATOM	711 CG LEU	86	10.554 12.687 9.712 12.313	3.114	1.00 22.96
	ATOM	712 CD1 LEU	86		1.902	1.00 28.74
35	ATOM	713 CD2 LEU	86		2.366	1.00 27.61
	ATOM	714 C LEU	86	9.425 13.575 12.480 13.973	1.084	1.00 29.85
	ATOM	715 O LEU	86	12.448 15.193	4.013	1.00 21.25
	ATOM	716 N LEU	87	12.965 13.213	4.089	1.00 21.77
	ATOM	717 CA LEU	87	13.510 13.821	4.986 6.196	1.00 22.23
<b>4</b> 0	ATOM	718 CB LEU	87	13.946 12.736	7.186	1.00 20.76
	ATOM	719 CG LEU	87	12.830 11.876	7.789	1.00 20.64
	ATOM	720 CD1 LEU	87	13.425 10.787	8.681	1.00 20.81 1.00 21.55
	MOTA	721 CD2 LEU	87	11.901 12.762	8.590	1.00 21.01
	ATOM	722 C LEU	87	14.696 14.727	5.860	1.00 21.15
<b>4</b> 5	MOTA	723 O LEU	87	14.808 15.842	6.367	1.00 21.87
	MOTA	724 N LEU	88	15.585 14.246	5.003	1.00 20.92
	ATOM	725 CA LEU	88	16.744 15.039	4.624	1.00 22.07
	ATOM	726 CB LEU	88	17.730 14.172	3.837	1.00 20.79
50	ATOM	727 CG LEU	88	18.572 13.279	4.759	1.00 24.02
30	ATOM	728 CD1 LEU	88	19.333 12.241	3.956	1.00 21.15
	ATOM	729 CD2 LEU	88	19.534 14.159	5.556	1.00 20.95
	ATOM	730 C LEU	88	16.380 16.293	3.831	1.00 22.47
	ATOM	731 O LEU	- 88	16.876 17.380	4.121	1.00 22.21
55	ATOM	732 N LYS	89	15.505 16.153	2.841	1.00 24.00
55	ATOM	733 CA LYS	89	15.106 17.303	2.028	1.00 25.58
	ATOM ATOM	734 CB LYS 735 CG LYS	89	14.174 16.855	0.897	1.00 28.38
	ATOM	735 CG LYS 736 CD LYS	89 89	13.626 18.006	0.053	1.00 33.25
	ATOM	737 CE LYS	89	12.677 17.499	-1.032	1.00 36.96
60	ATOM	738 NZ LYS	89	12.083 18.647 13.067 19.285	-1.857	1.00 40.68
	ATOM	739 C LYS	89	13.067 19.285 14.416 18.384	-2.776	1.00 41.21
	ATOM	740 O LYS	89	14.693 19.572	2.861	1.00 23.76
	ATOM	741 N SER	90	13.518 17.972	2.716	1.00 23.44
	ATOM	742 CA SER	90	12.806 18.943	3.745	1.00 24.58
65	ATOM	743 CB SER	90	11.462 18.359	4.559	1.00 24.92
	ATOM	744 OG SER	90	11.643 17.177	5.011	1.00 25.41
	ATOM	745 C SER	90	13.585 19.418	5.770	1.00 25.27
	ATOM	746 O SER	90	13.377 20.536	5.785	1.00 24.40
	ATOM	747 N GLY	91	14.493 18.587	6.255	1.00 24.10
<i>7</i> 0	MOTA	748 CA GLY	91	15.210 18.966	6.290 7.496	1.00 22.98 1.00 22.61
	ATOM	749 C GLY	91	16.696 19.258	7.496	
	ATOM	750 O GLY	91	17.268 19.627	8.473	1.00 23.29
	ATOM	751 N CYS	92	17.332 19.116	6.284	1.00 22.29 1.00 23.33
	ATOM	752 CA CYS	92	18.770 19.368	6.205	1.00 23.33
<i>7</i> 5	ATOM	753 CB CYS	92	19.291 19.140	4.781	1.00 26.18
	ATOM	754 SG CYS	92	18.549 20.198	3.516	1.00 25.18
	ATOM	755 C CYS	92	19.151 20.772	6.668	1.00 33.39
	ATOM	756 O CYS	92	20.073 20.938	7.467	1.00 20.78
00	ATOM	757 N LEU	93	18.442 21.782	6.176	1.00 20.74
80	ATOM	758 CA LEU	93	18.762 23.153	6.549	1.00 20.88
	ATOM	759 CB LEU	93	18.001 24.147	5.659	1.00 19.11
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			_				_		
	ATOM	760					05 615		
		760	CG	LEU	93	18.457		5.791	1.00 22.77
	ATOM	761		LEU	93	19.968	25.732	5.556	1.00 20.31
	ATOM	762	CD2	LEU	93	17.689	26.483	4.787	1.00 21.80
_	MOTA	763	С	LEU	93	18.478	23.427	8.024	1.00 20.09
5	MOTA	764	0	LEU	93	19.190	24.205		
_	ATOM	765						8.667	1.00 21.56
			N	GLU	94	17.452	22.788	8.568	1.00 18.63
	MOTA	766	CA	GLU	94	17.125	22.979	9.975	1.00 22.09
	ATOM	767	CB	GLU	94	15.813	22.273	10.335	1.00 20.52
	ATOM	768	CG	GLU	94	14.643	22.753		
10								9.497	1.00 23.52
10	MOTA	769	CD	GLU	94	13.303	22.276	10.027	1.00 24.62
	ATOM	770	OE1	GLU	94	13.285	,21.458	10.972	1.00 25.58
•	ATOM	771	OE2	GLU	94	12.268	22.724	9.492	1.00 26.18
	ATOM	772	С	GLU	94	18.267	22.440		
	MOTA	773						10.828	1.00 21.56
15			0	GLU	94	18.622	23.035	11.840	1.00 23.14
15	MOTA	774	N	VAL	95	18.847	21.315	10.419	1.00 22.47
	ATOM	775	CA	VAL	95	19.970	20.757	11.167	1.00 21.92
	ATOM	776	CB	VAL	95	20.358	19.348	10.660	
	MOTA	777							1.00 20.19
			CG1		95	21.640	18.884	11.347	1.00 17.76
20	ATOM	778	CG2	VAL	95	19.230	18.359	10.954	1.00 21.38
20	ATOM	779	С	VAL	95	21.179	21.690	11.043	1.00 20.91
	ATOM	780	0	VAL	95	21.891	21.921	12.022	
	ATOM	781	N						1.00 23.34
				VAL	96	21.419	22.219	9.843	1.00 20.72
	MOTA	782	CA	VAL	. 96	22.544	23.142	9.640	1.00 20.86
~=	ATOM	783	CB	VAL	96	22.632	23.609	8.168	1.00 20.89
25	ATOM	784	CG1		96	23.622	24.766	8.034	
	ATOM	785	CG2						1.00 21.60
					96	23.078	22.435	7.285	1.00 22.01
	MOTA	786	С	VAL	96	22.384	24.369	10.545	1.00 20.92
	ATOM	787	0	VAL	96	23.356	24.873	11.119	1.00 20.53
	MOTA	788	N	LEU	97	21.151	24.847		
30								10.672	1.00 21.56
50	ATOM	789	CA	LEU	97	20.879	26.008	11.507	1.00 22.41
	ATOM	790	CB	LEU	97	19.414	26.427	11.382	1.00 24.63
	ATOM	791	CG	LEU	97	19.039	27.746	12.062	1.00 27.57
	ATOM	792	CD1	LEU	97	19.785	28.888		
								11.375	1.00 27.68
35	ATOM	793		LEU	97	17.522	27.969	11.984	1.00 27.40
55	ATOM	794	С	LEU	97	21.196	25.687	12.963	1.00 23.37
	ATOM	795	0	LEU	97	21.774	26.510	13.670	1.00 24.02
	ATOM	796	N·	VAL	98	20.795	24.505		
	ATOM	797	CA	VAL				13.424	1.00 22.24
					98	21.083	24.124	14.801	1.00 22.66
40	ATOM	798	CB	VAL	98	20.454	22.753	15.168	1.00 24.14
40	MOTA	799	CG1	VAL	98	20.950	22.295	16.540	1.00 21.61
	ATOM	800	CG2	VAL	98	18.936	22.872	15.184	1.00 22.31
	ATOM	801	c	VAL	98	22.598			
							24.041	14.977	1.00 21.26
	ATOM	802	0	VAL	98	23.147	24.583	15.930	1.00 23.35
4 -	MOTA	803	N	ARG	. 99	23.275	23.381	14.043	1.00 21.04
45	ATOM	804	CA	ARG	99	24.728	23.238	14.126	1.00 22.66
	ATOM	805	СВ	ARG	99	25,241	22.338		
	ATOM	806						12.997	1.00 21.34
			CG	ARG	99	24.958	20.860	13.204	1.00 19.68
	ATOM	807	CD	ARG	99	25.493	20.040	12.042	1.00 20.91
<b>-</b> 0	ATOM	808	NE	ARG	99	25.596	18.628	12.392	1.00 19.97
50	ATOM	809	CZ	ARG	99	26.207	17.710	11.651	1.00 21.46
	MOTA	810		ARG	99				
						26.774	18.047	10.499	1.00 19.48
	ATOM	811		ARG	99	26.268	16.456	12.077	1.00 19.49
	ATOM	812	С	ARG	99	25.444	24.586	14.068	1.00 23.66
	ATOM	813	0	ARG	99	26.496	24.770	14.680	
55	ATOM	814	N	MET	•				1.00 22.32
-					100	24.873	25.524	13.325	1.00 24.98
	ATOM	815	CA	MET	100	25.468	26.849	13.200	1.00 26.11
	ATOM	816	CB	MET	100	24.580	27.732	12.315	1.00 24.69
	ATOM	817	CG	MET	100	25.125	29.131	12.096	1.00 28.62
	ATOM	818	SD	MET	100	23.935	30.203		
60								11.266	1.00 30.73
00	ATOM	819	CE	MET	100	22.917	30.695	12.620	1.00 28.23
	MOTA	820	С	MET	100	25.647	27.500	14.580	1.00 26.32
	ATOM	821	0	MET	100	26.560	28.303	14.791	1.00 25.50
	ATOM.	822	N	CYS	101	24.782	27.140		
	ATOM							15.524	1.00 26.14
65		823	CA	CYS	101	24.857	27.716	16.861	1.00 26.26
05	ATOM	824	CB	CYS	101	23.647	27.273	17.686	1.00 26.15
	ATOM	825	SG	CYS	101	22.070	27.833	16.958	1.00 28.21
	ATOM	826	c						
				CYS	101	26.155	27.369	17.579	1.00 26.31
	MOTA	827	0	CYS	101	26.556	28.064	18.512	1.00 27.18
70	ATOM	828	N	ARG	102	26.810	26.300	17.134	1.00 26.05
70	MOTA	829	CA	ARG	102	28.080	25.863	17.715	1.00 25.81
-	MOTA	830	СВ						
				ARG	102	28.487	24.477	17.194	1.00 24.97
	ATOM	831	CG	ARG	102	27.477	23.360	17.374	1.00 24.25
	ATOM	832	CD	ARG	102	27.899	22.131	16.567	1.00 24.77
	ATOM	833	NE	ARG	102	29.120	21.499	17.075	
<i>7</i> 5									1.00 24.27
, ,	ATOM	834	CZ	ARG	102	30.251	21.376	16.384	1.00 25.69
	MOTA	835	NH1	ARG	102	30.334	21.847	15.146	1.00 22.95
	ATOM	836	NH2	ARG	102	31.300	20.763	16.924	1.00 24.83
	ATOM	837	C	ARG	102	29.167	26.837	17.290	
									1.00 25.16
QΛ	MOTA	838	0	ARG	102	30.189	26.965	17.956	1.00 26.46
80	ATOM	839	N	ALA	103	28.949	27.499	16.158	1.00 25.50
	ATOM	840	CA	ALA	103	29.925	28.438	15.610	1.00 24.73

	ATOM	841 CB ALA	103	30 20	2 00 00		
	ATOM			30.28			
	ATOM		103	29.41			
	ATOM		103	29.66			
5	ATOM		104	28.70			1.00 24.81
J		845 CA PHE	104	28.13			1.00 24.87
	ATOM	846 CB PHE	104	26.61			1.00 24.62
	ATOM	847 CG PHE	104	25.91		16.868	
	ATOM	848 CD1 PHE	104	25.54		18.082	
10	MOTA	849 CD2 PHE	104	25.59	9 33.465	15.685	1.00 25.70
10	ATOM	850 CE1 PHE	104	24.87	6 34.610	18.115	1.00 27.97
	ATOM	851 CE2 PHE	104	24.93	0 34.693	15.708	
	ATOM	852 CZ PHE	104	24.56	8 35.263		1.00 25.05
	ATOM	853 C PHE	104	28.63	7 32.156		1.00 26.24
1 =	MOTA	854 O PHE	104	28.62	4 31.504		1.00 25.16
15	ATOM	855 N ASN	105	29.09			1.00 24.14
	ATOM	856 CA ASN	105	29.59			
	ATOM	857 CB ASN	105	30.833			1.00 25.15
	ATOM	858 CG ASN	105	31.414			1.00 25.27
	ATOM	859 OD1 ASN	105	30.811			1.00 28.22
20	ATOM	860 ND2 ASN	105				1.00 29.75
	ATOM	861 C ASN	105	32.592		19.853	1.00 28.02
	ATOM	862 O ASN		28.471		19.744	1.00 25.46
	ATOM		105	28.218		19.148	1.00 23.70
			106	27.784		20.835	1.00 26.30
25	ATOM	864 CD PRO	106	27.965		21.611	1.00 27.28
23	ATOM	865 CA PRO	106	26.680		21.382	1.00 27.94
	ATOM	866 CB PRO	106	25.995	34.442	22.339	1.00 27.49
	ATOM	867 CG PRO	106	27.150	33.646	22.867	1.00 27.98
	MOTA	868 C PRO	106	27.052	36.731		1.00 28.50
20	ATOM	869 O PRO	106	26.169		22.470	1.00 29.76
- 30	ATOM	870 N LEU	107	28.344		22.173	1.00 28.28
	ATOM	871 CA LEU	107	28.761		22.800	
	ATOM	872 CB LEU	107	30.150		23.444	1.00 30.25
	ATOM	873 CG LEU	107	30.176			1.00 28.28
	MOTA	874 CD1 LEU	107	31.562		24.686	1.00 31.14
35	ATOM	875 CD2 LEU	107	29.192		25.277	1.00 29.40
	ATOM	876 C LEU	107	28.758	37.746	25.726	1.00 32.31
	ATOM	877 O LEU	107	28.332	39.433	21.807	1.00 29.75
	ATOM	878 N ASN	107		40.533	22.142	1.00 31.64
	ATOM	879 CA ASN	108	29.231	39.193	20.589	1.00 28.78
<b>40</b>	ATOM			29.249	40.246	19.580	1.00 28.18
-0	ATOM		108	30.681	40.517	19.107	1.00 27.56
	ATOM		108	31.362	39.279	18.538	1.00 28.12
	ATOM		108	30.733	38.238	18.347	1.00 26.25
	ATOM	883 ND2 ASN	108	32.657	39.396	18.257	1.00 24.43
45		884 C ASN	108	28.364	39.894	18.386	1.00 27.75
10	MOTA	885 O ASN	108	28.432	40.537	17.343	1.00 27.33
	MOTA	886 N ASN	109	27.535	38.870	18.556	1.00 27.69
	ATOM	887 CA ASN	109	26.627	38.418	17.512	1.00 28.83
	ATOM	888 CB ASN	109	25.465	39.395	17.353	1.00 29.93
50	ATOM	889 CG ASN	109	24.546	39.387	18.543	1.00 32.72
30	ATOM	890 OD1 ASN	109	24.216	38.324	19.072	1.00 32.17
	MOTA	891 ND2 ASN	109	24.116	40.575	18.973	1.00 31.31
	ATOM	892 C ASN	109	27.293	38.222	16.164	1.00 27.63
	ATOM	893 O ASN	109	26.918	38.861	15.183	1.00 27.80
==	ATOM	894 N THR	110	28.287	37.342	16.124	1.00 26.91
55	ATOM	895 CA THR	110	28.990	37.042	14.889	
	ATOM	896 CB THR	110	30.469	37.468	14.967	1.00 26.50
	ATOM	897 OG1 THR	110	31.071	36.887	16.130	1.00 25.46
	ATOM	898 CG2 THR	110	30.587	38.987		1.00 24.60
	ATOM	899 C THR	110	28.908	35.535	15.050	1.00 26.91
60	ATOM	900 O THR	110	28.813		14.668	1.00 26.44
	ATOM	901 N. VAL	111	28.928	34.765	15.625	1.00 26.49
	ATOM	902 CA VAL	111		35.124	13.407	1.00 25.62
	ATOM	903 CB VAL		28.859	33.713	13.058	1.00 25.05
	ATOM		111	27.550	33.386	12.292	1.00 26.15
65	MOTA		111	27.581	34.012	10.893	1.00 25.65
00		905 CG2 VAL	111	27.364	31.875	12.207	1.00 25.76
	ATOM ATOM	906 C VAL	111	30.056	33.361	12.178	1.00 25.27
		907 O VAL	111	30.541	34.204	11.415	1.00 24.98
	ATOM	908 N LEU	112	30.536	32.126	12.302	1.00 23.55
70	ATOM	909 CA LEU	112	31.677	31.660	11.520	1.00 24.51
70	MOTA	910 CB LEU	112	32.171	30.316	12.067	1.00 24.17
	ATOM	911 CG LEU	112	33.323	29.570	11.384	1.00 26.81
	MOTA	912 CD1 LEU	112	34.579	30.439	11.321	
	ATOM	913 CD2 LEU	112	33.603	28.292	12.176	1.00 24.50
	ATOM	914 C LEU	112	31.251	31.512		1.00 26.23
<i>7</i> 5	ATOM	915 O LEU	112	30.347	30.734	10.063	1.00 25.07
	ATOM	916 N PHE	113	31.905	32.267	9.751	1.00 23.68
	ATOM	917 CA PHE	113	31.595	32.240	9.183	1.00 25.79
	ATOM	918 CB PHE	113	30.686		7.759	1.00 27.26
	ATOM	919 CG PHE	113	30.216	33.415	7.399	1.00 26.26
80	ATOM	920 CD1 PHE	113	29.338	33.399	5.975	1.00 26.51
-	ATOM	921 CD2 PHE	113		32.412	5.528	1.00 27.75
		ODE IND	-13	30.661.	34.358	5.073	1.00 26.90

	ATOM	922	CEI D	HE 113	20 016	22 200	4 100	
			CE1 P		28.910		4.199	1.00 27.83
	ATOM	923		HE 113	30.239		3.736	1.00 27.68
	ATOM	924	CZ P	HE 113	29.361	33.344	3.302	1.00 26.77
_	ATOM	925	C PI	HE 113	32.885	32.318	6.954	1.00 28.10
5	ATOM	926		HE 113	33.651		7.079	1.00 29.91
-	ATOM	927		LU 114	33.117		6.122	
								1.00 30.65
	MOTA	928		LU 114	34.325	_	5.312	1.00 31.06
	MOTA	929	CB G	LU 114	34.296	32.295	4.188	1.00 30.36
	ATOM	930	CG G	LU 114	33.108	32.146	3.220	1.00 33.61
10	ATOM	931		LU 114	33.194	33.074	2.006	1.00 36.26
	ATOM	932	OE1 G			34.137		
					33.847		2.098	1.00 37.14
	ATOM	933	OE2 G	-	32.596		0.960	1.00 36.76
	MOTA	934	C G	LU 114	35.579	31.416	6.169	1.00 31.09
	MOTA	935	O G!	LU 114	36.425	32.267	5.893	1.00 29.44
15	ATOM	936	N G	LY 115	35.678	30.619	7.232	1.00 31.65
	ATOM	937	CA GI		36.862	30.653		
							8.077	1.00 31.02
	ATOM	938	C GI		36.987	31.636	9.227	1.00 31.03
	ATOM	939	O GI	LY 115	37.850	31.453	10.081	1.00 31.02
	ATOM	940	N L	rs 116	36.165	32.678	9.266	1.00 30.47
20	MOTA	941	CA L		36.247	33.640	10.364	1.00 29.13
	ATOM	942	CB L		37.081	34.850	9.950	
								1.00 31.65
	ATOM	943	CG L		38.518	34.542	9.546	1.00 35.17
	MOTA	944	CD L		39.156	35784	8.933	1.00 39.50
~=	ATOM	945	CE L	(S 116	40.598	35.550	8.517	1.00 41.93
25	MOTA	946	NZ L	rs 116	41.482	35.336	9.699	1.00 46.16
	ATOM	947	C L		34.855	34.108	10.773	1.00 28.58
	ATOM	948						
					33.883	33.914	10.035	1.00 25.83
	MOTA	949	N T		34.773	34.731	11.947	1.00 26.38
~~	ATOM	950	CA T	r 117	33.513	35.241	12.473	1.00 26.28
30	MOTA	951	CB TY	(R 117	33.557	35.311	14.006	1.00 27.82
	ATOM	952	CG TY		33.470	33.964	14.684	1.00 25.87
	ATOM	953	CD1 TY					
					34.524	33.048	14.605	1.00 27.04
	MOTA	954	CE1 TY		34.426	31.782	15.190	1.00 26.50
0.5	ATOM	955	CD2 TY	r 117	32.316	33.585	15.369	1.00 23.65
35	MOTA	956	CE2 TY	(R 117	32.208	32.329	15.953	1.00 26.33
	ATOM	957	CZ TY		33.263	31.433	15.858	1.00 26.31
	ATOM	958	OH TY		33.136	30.179		
							16.405	1.00 29.08
	MOTA	959	C TY		33.191	36.624	11.922	1.00 27.89
40	MOTA	960	O T		34.063	37.491	11.837	1.00 27.82
<b>4</b> 0	ATOM	961	N GI	LY 118	31.932	36.821	11.551	1.00 27.62
	ATOM	962	CA GI	Y 118	31.503	38.104	11.029	1.00 27.35
	ATOM	963	C GI		30.086	38.415	11.476	1.00 27.40
	MOTA	964						
				Y 118	29.275	37.502	11.644	1.00 26.12
45	ATOM	965	N GI		29.787	39.698	11.673	1.00 27.51
45	ATOM	966	CA GI	Y 119	28.455	40.092	12.104	1.00 28.25
	ATOM	967	C GI	Y 119	27.465	39.994	10.964	1.00 30.48
	ATOM	968	O GI	Y 119	27.845	39.624	9.852	1.00 32.66
	ATOM	969	N ME		26,203	40.328	11.215	
	ATOM	970						
50					25.200	40.245	10.159	1.00 33.29
50	ATOM	971	CB ME		23.786	40.417	10.742	1.00 35.95
	ATOM	972	CG ME	ET 120	23.464	41.793	11.321	1.00 40.01
	ATOM	973	SD ME	ET 120	23.194	43.077	10.066	1.00 44.66
	ATOM	974	CE ME	T 120	21.580	42.608	9.449	1.00 38.51
	ATOM	975	C ME		25.423	41.233	9.010	1.00 33.96
55								
55	ATOM	976	O ME		24.889	41.036	7.916	1.00 32.84
	MOTA	977	N GI		26.218	42.280	9.245	1.00 34.68
	ATOM	978	CA GI	LN 121	26.489	43.281	8.209	1.00 36.23
	MOTA	979	CB GI	N 121	27.204	44.509	8.794	1.00 37.39
	ATOM	980	CG GI		28.683	44.292	9.088	1.00 40.21
60	ATOM	981	CD GI		28.930	43.759		
00		982					10.485	1.00 42.57
	ATOM		OE1 GI		28.035	43.184	11.111	1.00 42.30
	MOTA	983	NE2 GI		30.154	43.943	10.982	1.00 43.39
	MOTA	984	C GI	N 121	27.357	42.670	7.117	1.00 36.52
	ATOM	985	O GI	N 121	27.577	43.263	6.062	1.00 38.05
65	ATOM	986	N ME		27.852	41.474	7.397	1.00 35.28
	ATOM	987	CA ME		28.686			
						40.731	6.474	1.00 32.99
•	ATOM	988	CB ME		29.324	39.562	7.239	1.00 34.32
	MOTA	989	CG ME		30.068	38.536	6.417	1.00 32.66
70	MOTA	990	SD ME	T 122	31.016	37.409	7.491	1.00 32.03
<i>7</i> 0	ATOM	991	CE ME		29.704	36.572	8.406	1.00 29.49
-	ATOM	992	C ME		27.819			
						40.225	5.317	1.00 33.06
	ATOM	993	O ME		28.315	39.986	4.219	1.00 31.80
	MOTA	994	N PH		26.519	40.094	5.571	1.00 31.66
	MOTA	995	CA PH	IE 123	25.565	39.596	4.580	1.00 32.27
<i>7</i> 5	ATOM	996	CB PH		24.640	38.567	5.235	1.00 29.78
	ATOM	997	CG PI		25.366	37.400	5.838	1.00 30.41
	ATOM	998	CD1 PI		25.875	36.387	5.030	1.00 28.95
	MOTA	999	CD2 PF		25.553	37.318	7.213	1.00 28.84
00	ATOM	1000	CE1 PH		26.556	35.307	5.586	1.00 28.63
80	ATOM	1001	CE2 PH		26.234	36.243	7.779	1.00 28.70
0								
	ATOM	1002	CZ PI	E 123	26.736	35.235	6.965	1.00 29.76

							03		
	ATOM	1003	С	PHE	123	24.709	40.695	3.952	1.00 33.01
	MOTA	1004		PHE	123	23.671	40.410	3.352	1.00 32.84
	MOTA MOTA	1005 1006		LYS LYS	124 124	25.149	41.941	4.082	1.00 33.57
5	MOTA	1007			124	24.409 25.228	43.075 44.361	3.542 3.737	1.00 35.39
	ATOM	1008			124	24.439	45.645	3.501	1.00 38.66 1.00 43.12
	ATOM	1009			124	23.162	45.650	4.341	1.00 46.67
	ATOM	1010			124	22.286	46.866	4.040	1.00 49.30
10	ATOM ATOM	1011 1012		LYS LYS	124 124	20.975 24.005	46.787	4.753	1.00 48.16
10	ATOM	1013		LYS	124	22.858	42.923 43.169	2.071 1.719	1.00 33.97
	MOTA	1014	N	ALA	125	24.936	42.497	1.219	1.00 34.76 1.00 34.80
	ATOM	1015	CA	ALA	125	24.666	42.347	-0.215	1.00 34.52
15	ATOM	1016	CB	ALA	125	25.955	41.965	-0.953	1.00 33.38
15	ATOM ATOM	1017 1018	С 0	ALA ALA	125 125	23.548 23.125	41.366	-0.583	1.00 35.75
	ATOM	1019	N	LEU	126	23.123	41.313	-1.738 0.378	1.00 35.49 1.00 35.88
	ATOM	1020	CA	LEU	126	21.993	39.640	0.085	1.00 35.88
20	ATOM	1021	СВ	LEU	126	21.877	38.583	1.181	1.00 34.67
20	ATOM ATOM	1022 1023	CG	LEU	126	23.019	37.586	1.309	1.00 33.16
	ATOM	1023		LEU LEU	126 126	22.701 23.200	36.629 36.831	2.442	1.00 33.20
	ATOM	1025	Č.	LEU		20.661	40.360	-0.006 -0.037	1.00 31.66 1.00 35.66
OF.	ATOM	1026	O	LEU	126	19.745	39.881	-0.699	1.00 37.30
25	ATOM	1027	N	GLY	127	20.556	41.509	0.618	1.00 36.88
	ATOM	1028	CA	GLY	127	19.319	42.261	0.577	1.00 37.45
	ATOM ATOM	1029 1030	C O	GLY	127 127	18.231	41.495	1.295	1.00 38.00
	ATOM	1031	N	SER	128	17.047 18.637	41.645 40.672	0.992 2.257	1.00 37.47
30	ATOM	1032	CA	SER	128	17.696	39.862	3.024	1.00 38.76 1.00 38.85
	ATOM	1033	CB	SER	128	17.783	38.399	2.575	1.00 39.65
	ATOM	1034	OG	SER	128	17.675	38.280	1.167	1.00 40.93
	ATOM ATOM	1035 1036	c o	SER SER	128	18.004	39.946	4.518	1.00 38.88
35	ATOM	1037	N	ASP	128 129	18.142 18.104	38.916 41.160	5.184	1.00 38.92
	ATOM	1038	CA	ASP	129	18.413	41.327	5.050 6.469	1.00 38.31 1.00 37.76
	ATOM	1039	CB	ASP	129	18.513	42.809	6.837	1.00 38.81
	ATOM	1040	CG	ASP	129	19.785	43.458	6.322	1.00 37.85
<b>4</b> 0	ATOM ATOM	1041 1042	OD1		129 129	20.698 19.877	42.734	5.884	1.00 39.00
	ATOM	1043	C	ASP	129	17.399	44.700 40.651	6.369 7.382	1.00 40.89 1.00 37.23
	MOTA	1044	0	ASP	129	17.734	40.238	8.490	1.00 37.23 1.00 36.42
	MOTA	1045	N	ASP	130	16.156	40.542	6.930	1.00 36.72
45	ATOM ATOM	1046	CA	ASP	130	157143	39.901	7.755	1.00 36.80
10	ATOM	1047 1048	CB CG	ASP ASP	130 130	13.760 13.722	40.044 39.535	7.110	1.00 38.13
	MOTA	1049		ASP	130	14.726	39.717	5.688 4.969	1.00 40.50 1.00 40.76
	ATOM	1050	OD2		130	12.680	38.969	5.285	1.00 41.30
50	ATOM	1051	Ç	ASP	130	15.507	38.430	7.958	1.00 34.04
50	ATOM ATOM	1052 1053	N N	ASP LEU	130	15.376	37.899	9.058	1.00 32.59
	ATOM	1054	CA	LEU	131 131	15.974 16.368	37.779 36.380	6.897	1.00 31.60
	ATOM	1055	CB	LEU	131	16.735	35.812	6.994 5.615	1.00 29.28 1.00 28.37
55	ATOM	1056	CG	LEU	131	17.529	34.490	5.653	1.00 28.49
33	ATOM	1057		LEU	131	16.701	33.410	6.352	1.00 26.24
	MOTA MOTA	1058 1059	CD2	LEU LEU	131 131	17.895	34.046	4.249	1.00 25.43
	ATOM	1060	ŏ	LEU	131	17.569 17.560	36.270 35.495	7.924 8.882	1.00 28.88
<b>60</b>	ATOM	1061	N	VAL	132	18.603	37.058	7.646	1.00 28.78 1.00 28.88
60	ATOM	1062	CA	VAL	132	.19.805	37.032	8.473	1.00 28.97
	ATOM	1063	CB	VAL	132	20.843	38.038	7.953	1.00 28.69
	ATOM ATOM	1064 1065	CG1	VAL	132	22.086	37.998	8.822	1.00 27.42
	ATOM	1066	C	VAL VAL	132 132	21.195 19.490	37.706 37.319	6.512	1.00 29.10
65	ATOM	1067	ŏ	VAL	132	19.912	36.571	9.943 10.831	1.00 29.17 1.00 29.93
	ATOM	1068	N	ASN	133	18.748	38.395	10.198	1.00 29.09
	ATOM	1069	CA	ASN	133	18.367	38.759	11.562	1.00 28.91
	MOTA	1070	CB	ASN	133	17.477	40.004	11.552	1.00 31.79
70	ATOM ATOM	1071 1072	CG	ASN ASN	133 133	18.275	41.297	11.466	1.00 35.19
	ATOM	1073		ASN	133	17.728 19.569	42.352	11.149 11.765	1.00 36.03
	ATOM	1074	C	ASN	133	17.634	37.620	12.266	1.00 34.40 1.00 28.71
	ATOM	1075	0	ASN	133	17.850	37.376	13.453	1.00 28.71
<i>7</i> 5	ATOM	1076	N	GLU	134	16.758	36.928	11.546	1.00 27.60
15	ATOM	1077	CA	GLU	134	16.033	35.815	12.154	1.00 29.70
	MOTA MOTA	1078 1079	CB CG	GLU GLU	134 134	14.904	35.340	11.235	1.00 30.25
	ATOM	1079	CD	GLU	134	13.612 12.429	36.130 35.572	11.441 10.672	1.00 37.54
00	ATOM	1081		GLU	134	12.311	34.333	10.572	1.00 39.03 1.00 42.45
80	MOTA	1082	OE2	GLU	134	11.604	36.376	10.186	1.00 43.40
	ATOM	1083	С	GLU	134	16.978	34.659	12.484	1.00 28.63

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	ATOM	1084	0	GLU	134	16.867	34.040	13.540	1 00 27 52
	ATOM	1085	Ŋ	ALA	135	17.916	34.385	11.583	1.00 27.53
	ATOM	1086	CA	ALA	135	18.887	33.317	11.791	1.00 28.23 1.00 27.00
_	ATOM	1087	СВ	ALA	135	19.769	33.178	10.571	1.00 27.00
5	MOTA	1088	С	ALA	135	19.734	33.636	13.019	1.00 27.05
	ATOM	1089	0	ALA	135	19.955	32.774	13.876	1.00 25.93
	ATOM	1090	N	PHE	136	20.199	34.881	13.104	1.00 27.53
	ATOM	1091	CA	PHE	136	21.018	35.322	14.229	1.00 28.38
10	MOTA	1092	CB	PHE	136	21.569	36.728	13.963	1.00 29.04
10	ATOM	1093	CG	PHE	136	22.817	36.742	13.123	1.00 27.20
	MOTA	1094	CD1	PHE	136	22.858	36.084	11.898	1.00 28.97
	ATOM	1095	CD2		136	23.954	37.422	13.555	1.00 28.84
	MOTA	1096	CEI	PHE	136	24.014	36.103	11.114	1.00 28.21
1 🖺	ATOM	1097	CE2	PHE	136	25.117	37.446	12.776	1.00 27.38
15	MOTA	1098	CZ	PHE	136	25.143	36.785	11.555	1.00 27.06
	ATOM	1099	C	PHE	136	20.278	35.306	15.566	1.00 29.12
	MOTA	1100	0	PHE	136	20.834	34.876	16.581	1.00 27.78
	MOTA	1101	N	ASP	137	19.031	35.772	15.573	1.00 30.75
20	MOTA	1102	CA	ASP	137	18.247	35.798	16.808	1.00 31.48
20	MOTA	1103	CB	ASP	137	16.888	36.463	16.570	1.00 34.88
	ATOM	1104	CG	ASP	137	17.013	37.938	16.197	1.00 39.69
	ATOM ATOM	1105 1106	OD2	ASP	137	18.118	38.513	16.338	1.00 41.72
	MOTA	1107	C	ASP ASP	137 137	15.997	38.524 34.388	15.769	1.00 41.77
25	ATOM	1108	ŏ	ASP	137	18.046 18.094	34.173	17.361	1.00 30.07
	MOTA	1109	N	PHE	138	17.814	33.430	18.572 16.470	1.00 28.12
	ATOM	1110	CA	PHE	138	17.635	32.043	16.888	1.00 29.22
	ATOM	1111	СВ	PHE	138	17.284	31.156		1.00 27.56 1.00 26.66
	ATOM	1112	CG	PHE	138	17.481	29.693	15.964	1.00 27.08
30	ATOM	1113	CD1	PHE	138	16.631	29.018	16.833	1.00 27.62
	ATOM	1114	CD2	PHE	138	18.562	29.010	15.414	1.00 25.94
	ATOM	1115	CE1	PHE	138	16.854	27.679	17.157	1.00 27.42
	ATOM	1116	CE2	PHE	138	18.798	27.671	15.731	1.00 26.61
0.5	MOTA	1117	CZ	PHE	138	17.942	27.005	16.606	1.00 27.10
35	ATOM	1118	C	PHE	138	18.931	31.524	17.520	1.00 26.65
	MOTA	1119	0	PHE	138	18.932	30.996	18.638	1.00 25.79
	MOTA	1120	N	ALA	139	20.028	31.673	16.783	1.00 26.86
	ATOM	1121	CA	ALA	139	21.335	31.228	17.246	1.00 28.26
40	ATOM	1122	CB	ALA	139	22.409	31.620	16.246	1.00 24.42
40	ATOM	1123	c	ALA	139	21.629	31.854	18.598	1.00 29.32
	ATOM	1124	0	ALA	139	22.062	31.175	19.523	1.00 29.76
	ATOM ATOM	1125 1126	N	LYS	140	21.388	33.154	18.705	1.00 30.35
	ATOM	1127	CA CB	LYS LYS	140 140	21.628	33.857	19.955	1.00 33.43
45	ATOM	1128	CG	LYS	140	21.305 21.512	35.345 36.156	19.795	1.00 35.05
	ATOM	1129	CD	LYS	140	21.304	37.645	21.056 20.808	1.00 41.64
	ATOM	1130	CE	LYS	140	21.412	38.426	22.113	1.00 45.36 1.00 48.64
	ATOM	1131	NZ	LYS	140	22.648	38.062	22.869	1.00 48.83
=-	ATOM	1132	С	LYS	140	20.784	33.250	21.072	1.00 32.60
50	MOTA	1133	0	LYS	140	21.271	33.018	22.173	1.00 33.54
	ATOM	1134	N	ASN	141	19.520	32.968	20.782	1.00 33.89
	ATOM	1135	CA	ASN	141	18.645	32.397	21.794	1.00 34.26
	ATOM	1136	CB	ASN	141	17.187	32.488	21.351	1.00 35.65
55	ATOM	1137	CG	ASN	141	16.714	33.922	21.246	1.00 41.37
55	ATOM	1138	OD1		141	17.033	34.759	22.102	1.00 41.73
	ATOM	1139	ND2		141	15.944	34.218	20.203	1.00 43.55
	ATOM ATOM	1140	С 0	ASN	141	18.993	30.961	22.155	1.00 32.74
	ATOM	1141 1142	N	ASN LEU	141 142	18.857 19.439	30.565	23.307	1.00 32.51
60	ATOM	1143	CA	LEU	142	19.800	30.178 28.800	21.180	1.00 31.43
••	ATOM	1144	CB	LEU	142	20.061	28.009	21.475 20.190	1.00 29.57
	ATOM	1145	CG	LEU	142	20.302	26.512	20.190	1.00 31.15 1.00 30.62
	ATOM	1146	CD1		142	19.000	25.852	20.835	1.00 30.62
	ATOM	1147	CD2		142	20.824	25.870	19.149	1.00 28.71
65	ATOM	1148	С	LEU	142 .	21.058	28.809	22.329	1.00 28.67
	ATOM	1149	0	LEU	142	21.188	28.022	23.266	1.00 27.68
	ATOM	1150	N	CYS	143	21.988	29.706	22.004	1.00 28.64
	MOTA	1151	CA	CYS	143	23.240	29.805	22.751	1.00 28.53
70	MOTA	1152	CB	CYS	143	24.164	30.857	22.118	1.00 29.40
70	MOTA	1153	SG	CYS	143	25.058	30.297	20.626	1.00 30.27
	ATOM	1154	С	CYS	143	23.011	30.141	24.225	1.00 28.51
	ATOM	1155	0	CYS	143	23.811	29.764	25.083	1.00 27.46
	ATOM	1156	N	SER	144	21.922	30.844	24.524	1.00 27.47
75	ATOM	1157	CA	SER	144	21.631	31.204	25.907	1.00 30.41
75	ATOM	1158	СВ	SER	144	20.407	32.123	25.978	1.00 30.97
	ATOM	1159	OG	SER	144	19.221	31.404	25.687	1.00 32.16
	ATOM	1160	C	SER	144	21.391	29.963	26.776	1.00 30.53
	ATOM	1161	0	SER	144	21.527	30.024	27.995	1.00 31.62
80	ATOM	1162	N	LEU	145	21.039	28.841	26.147	1.00 29.38
00	ATOM	1163	CA	LEU	145	20.787	27.600	26.878	1.00 28.47
	MOTA	1164	CB	LEU	145	19.886	26.664	26.062	1.00 30.06

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	ATOM	1165	CG	LEU	145	18.452	27.120	25.776	1.00 30.81
	ATOM ATOM	1166 1167	CD2	LEU	145	17.736	26.074	24.929	1.00 31.42
	ATOM	1168	C	LEU	145 145	17.711 22.078	27.326 26.869	27.092 27.242	1.00 32.81
5	ATOM	1169	0	LEU	145	22.060	25.936	28.041	1.00 27.00 1.00 26.93
	ATOM	1170	N	GLN	146	23.192	27.285	26.647	1.00 27.19
	MOTA MOTA	1171 1172	CA CB	GLN GLN	146 146	24.481 24.912	26.669	26.938	1.00 28.35
	MOTA	1173	CG	GLN	146	25.051	27.015 28.488	28.364 28.638	1.00 31.85 1.00 37.93
10	MOTA	1174	CD	GLN	146	26.153	29.120	27.823	1.00 43.03
	ATOM	1175	OE1		146	27.326	28.736	27.920	1.00 45.91
	MOTA MOTA	1176 1177	NE2 C	GLN GLN	146 146	25.785 24.451	30.096 25.147	27.005	1.00 46.57
<b>-</b> -	ATOM	1178	ŏ	GLN	146	24.803	24.425	26.797 27.738	1.00 28.31 1.00 28.78
15	ATOM	1179	N	LEU	147	24.035	24.657	25.634	1.00 24.96
	MOTA MOTA	1180 1181	CA CB	LEU	147 147	23.971	23.219	25.405	1.00 25.05
	ATOM	1182	CG	LEU	147	23.129 21.682	22.919 23.401	24.166 24.168	1.00 24.70 1.00 25.61
20	ATOM	1183	CD1	LEU	147	21.020	22.977	22.858	1.00 27.01
20	ATOM	1184		LEU	147	20.945	22.817	25.369	1.00 26.03
	ATOM ATOM	1185 1186	C O	LEU LEU	147 147	25.357 26.253	22.616 23.262	25.206	1.00 25.19
	ATOM	1187	N	THR	148	25.533	21.377	24.664 25.650	1.00 25.02 1.00 25.71
25	ATOM	1188	CA	THR	148	26.809	20.697	25.473	1.00 25.53
25	ATOM ATOM	1189 1190	CB OG1	THR	148	27.004	19.561	26.495	1.00 25.85
	ATOM	1191	CG2		148 148	25.986 26.933	18.572 20.101	26.297 27.937	1.00 25.37 1.00 25.32
	ATOM	1192	C	THR	148	26.777	20.078	24.076	1.00 25.32
30	ATOM	1193	0	THR	148	25.741	20.098	23.395	1.00 23.91
50	ATOM ATOM	1194 1195	N CA	GLU GLU	149 149	27.906 27.973	19.528 18.898	23.647	1.00 24.54
	ATOM	1196	CB	GLU	149	29.420	18.498	22.335 22.007	1.00 25.20 1.00 24.58
	ATOM	1197	CG	GLU	149	30.257	19.657	21.475	1.00 27.87
35	MOTA MOTA	1198 1199	CD OE1	GLU	149 149	29.926 30.532	20.009	20.024	1.00 28.51
	ATOM	1200	OE2		149	29.053	19.410 20.877	19.113 19.794	1.00 28.15 1.00 30.62
	ATOM	1201	С	GLU	149	27.052	17.684	22.268	1.00 24.09
	MOTA MOTA	1202 1203	о И	GLU GLU	149 150	26.472	17.403	21.225	1.00 26.05
<b>4</b> 0	ATOM	1204	CA	GLU	150	26.904 26.034	16.968 15.789	23.377 23.393	1.00 24.30 1.00 24.51
	ATOM	1205	CB	GLU	1,50	26.163	15.027	24.712	1.00 24.35
	ATOM ATOM	1206 1207	CG CD	GLU	150	27.526	14.403	24.987	1.00 28.10
	MOTA	1208		GLU	150 150	27.522 26.883	13.586 14.030	26.280 27.258	1.00 31.06
45	ATOM	1209	OE2	GLU	150	28.154	12.507	26.322	1.00 23.30
	ATOM ATOM	1210 1211	C O	GLU GLU	150 150	24.571	16.189	23.211	1.00 24.19
	ATOM	1212	N	GLU	151	23.807 24.187	15.500 17.300	22.529 23.833	1.00 24.28 1.00 23.86
50	ATOM	1213	CA	GLU	151	22.818	17.787	23.757	1.00 23.65
30	ATOM ATOM	1214 1215	CB CG	GLU	151	22.595	18.871	24.816	1.00 23.47
	ATOM	1216	CD	GLU GLU	151 151	22.812 22.835	18.336 19.420	26.238 27.300	1.00 23.24 1.00 25.20
	ATOM	1217		GLU	151	23.196	20.573	26.977	1.00 25.28
55	ATOM ATOM	1218 1219		GLU	151	22.505	19.111	28.466	1.00 25.81
00	ATOM	1220	C O	GLU GLU	151 151	22.524 21.432	18.311 18.113	22.358	1.00 24.05
	ATOM	1221	N	ILE	152	23.510	18.968	21.833 21.751	1.00 22.27 1.00 23.71
	ATOM	1222	CA	ILE	152	23.342	19.487	20.406	1.00 24.39
60	MOTA MOTA	1223 1224	CB CG2	ILE	152 152	24.538 24.545	20.358 20.559	19.996 18.484	1.00 26.20
	MOTA	1225		ILE	152	24.461	21.699	20.732	1.00 27.07 1.00 27.68
	ATOM	1226	CD1		152	25.778	22.469	20.758	1.00 32.87
	ATOM ATOM	1227 1228	C O	ILE	152 152	23.208 22.394	18.318	19.440	1.00 24.33
65	ATOM	1229	N	ALA	153	24.007	18.346 17.282	18.515 19.666	1.00 24.36 1.00 22.40
	MOTA	1230	CA	ALA	153	23.968	16.097	18.821	1.00 21.95
	ATOM ATOM	1231 1232	CB C	ALA	153	25.004	15.076	19.311	1.00 20.15
	ATOM	1233	ŏ	ALA ALA	153 153	22.578 21.965	15.471 15.238	18.836 17.788	1.00 19.88
70	MOTA	1234	N	LEU	154	22.092	15.199	20.037	1.00 20.80 1.00 19.09
	ATOM	1235	CA	LEU	154	20.794	14.573	20.222	1.00 21.33
	ATOM ATOM	1236 1237	CB CG	LEU LEU	154 154	20.604 21.616	14.206	21.699	1.00 21.40
75	ATOM	1238	CD1		154	21.415	13.184 12.961	22.230 23.728	1.00 24.62 1.00 25.79
75	ATOM	1239	CD2	LEU	154	21.448	11.878	21.472	1.00 25.80
	ATOM	1240 1241	C	LEU	154	19.653	15.456	19.730	1.00 21.75
	ATOM ATOM	1241	N N	LEU Phe	154 155	18.742 19.706	14.979 16.744	19.044 20.061	1.00 20.76 1.00 21.95
90	ATOM	1243	CA	PHE	155	18.662	17.654	19.621	1.00 21.95
80	ATOM	1244	CB	PHE	155	18.826	19.038	20.250	1.00 22.84
	MOTA	1245	CG	PHE	155	17.755	20.007	19.841	1.00 24.22

	MOTA	1246	CD:	1 PHE	155	16.419	19.737	20.107	1.00 25.61
•	MOTA MOTA	1247 1248		PHE PHE	155 155	18.077 15.415	21.187 20.636	19.186 19.723	1.00 24.20
_	ATOM	1249		PHE	155	17.087	22.088	18.800	1.00 25.64 1.00 24.91
5	MOTA MOTA	1250 1251	CZ C	PHE	155	15.753	21.812	19.069	1.00 24.00
	ATOM	1252	Ö	PHE	155 155	18.654 17.595	17.792 17.740	18.104 17.481	1.00 22.70 1.00 23.42
	ATOM	1253	N	SER	156	19.824	17.967	17.502	1.00 22.39
10	ATOM ATOM	1254 1255	CA CB	SER SER	156 156	19.873 21.308	18.105 18.330	16.053 15.565	1.00 21.92 1.00 23.31
	MOTA	1256	OG	SER	156	22.097	17.163	15.712	1.00 23.31
	MOTA MOTA	1257 1258	С 0	SER SER	156 156	19.290	16.853	15.407	1.00 20.69
	ATOM	1259	N	SER	157	18.632 19.508	16.939 15.692	14.378 16.020	1.00 21.06 1.00 19.99
15	ATOM	1260	CA	SER	157	18.974	14.456	15.462	1.00 20.74
	ATOM ATOM	1261 1262	CB OG	SER SER	157 157	19.609 19.026	13.232 12.965	16.139 17.405	1.00 20.43 1.00 22.34
	ATOM	1263	С	SER	157	17.443	14.403	15.596	1.00 21.96
20	ATOM ATOM	1264 1265	о И	SER ALA	157 158	16.759 16.907	13.833 14.994	14.739	1.00 20.32
20	ATOM	1266	CA	ALA	158	15.453	15.015	16.663	1.00 21.59 1.00 23.00
	ATOM	1267	CB	ALA	158	15.111	15.494	18.284	1.00 22.43
	ATOM ATOM	1268 1269	C O	ALA ALA	158 158	14.815 13.707	15.939 15.690	15.837 15.366	1.00 22.79 1.00 24.41
25	ATOM	1270	N	VAL	159	15.519	17.012	15.494	1.00 22.53
	ATOM ATOM	1271 · 1272	CA	VAL VAL	159 159	15.037 15.997	17.965	14.497	1.00 21.80
	ATOM	1273		VAL	159	15.670	19.175 20.003	14.393 13.162	1.00 21.36 1.00 23.95
30	ATOM	1274		VAL	159	15.877	20.036	15.649	1.00 19.81
50	MOTA MOTA	1275 1276	C O	VAL VAL	159 159	14.945 13.981	17.257 17.434	13.143 12.390	1.00 22.32 1.00 22.54
	ATOM	1277	N	LEU	160	15.946	16.429	12.861	1.00 20.50
	ATOM ATOM	1278 1279	CA CB	LEU LEU	160 160	16.011 17.416	15.661 15.067	11.622	1.00 21.56
35	ATOM	1280	CG	LEU	160	17.565	14.114	11.443 10.252	1.00 18.74
	ATOM ATOM	1281 1282		LEU	160	17.342	14.880	8.962	1.00 23.67
	ATOM	1283	CD2	LEU .	160 160	18.944 14.988	13.466 14.523	10.269 11.574	1.00 22.07 1.00 22.22
40	ATOM	1284	0	LEU	160	14.305	14.336	10.569	1.00 23.99
40	ATOM ATOM	1285 1286	N CA	ILE ILE	161 161	14.906 13.982	13.753 12.622	12.654 12.723	1.00 24.28 1.00 24.95
	ATOM	1287	CB	ILE	161	14.492	11.534	13.712	1.00 24.95
	ATOM ATOM	1288 1289		ILE	161 161	13.739 15.993	10.234	13.494	1.00 24.65
45	ATOM	1290		ILE	161	16.372	11.289 10.830	13.515 12.152	1.00 29.20 1.00 31.88
	ATOM ATOM	1291 1292	C	ILE	161	12.632	13.136	13.203	1.00 23.52
	ATOM	1293	N N	ILE SER	161 162	12.214 11.966	12.852 13.909	14.327 12.347	1.00 22.05 1.00 23.68
50	ATOM	1294	CA	SER	162	10.671	14.482	12.681	1.00 24.76
50	ATOM ATOM	1295 1296	CB OG	SER SER	162 162	10.612 9.274	15.946 16.413	12.264 12.349	1.00 23.48
	MOTA	1297	С	SER	162	9.514	13.742	12.030	1.00 25.92
	ATOM ATOM	1298 1299	O N	SER PRO	162 163	9.393 8.630	13.707	10.810	1.00 23.88
55	ATOM	1300	CD	PRO	163	8.685	13.154 13.100	12.848 14.321	1.00 28.81 1.00 28.18
	ATOM ATOM	1301 1302	CA CB	PRO	163		12.411	12.333	1.00 29.09
	ATOM	1303	CG	PRO PRO	163 163	7.018 7.318	11.612 12.553	13.546 14.684	1.00 28.39
60	ATOM	1304	C	PRO	163	6.375	13.312	11.786	1.00 30.74
00	ATOM ATOM	1305 1306	N	PRO ASP	163 164	5.354 6.586	12.824 14.624	11.297 11.851	1.00 31.15 1.00 31.09
	MOTA	1307	CA	ASP	164	5.582	15.563	11.371	1.00 32.86
	ATOM ATOM	1308 1309	CB CG	ASP ASP	164 164	5.494 5.004	16.768 16.383	12.309	1.00 35.68
65	ATOM	1310		ASP	164	3.928	15.754	13.697 13.790	1.00 41.26 1.00 42.32
	ATOM	1311 1312		ASP	164	5.691	16.704	14.692	1.00 44.22
	ATOM ATOM	1312	C O	ASP ASP	164 164	5.788 4.929	16.038 16.727	9.942 9.394	1.00 31.89 1.00 31.96
70	ATOM	1314	N	ARG	165	6.910	15.665	9.333	1.00 29.36
70	ATOM ATOM	1315 1316	CA CB	ARG ARG	165 165	7.184	16.073	7.963	1.00 28.58
	ATOM	1317	CG	ARG	165	8.525 9.732	15.507 15.898	7.477 8.313	1.00 25.79 1.00 24.11
	ATOM	1318	CD	ARG	165	9.861	17.404	8.460	1.00 20.61
75	ATOM ATOM	1319 1320	NE CZ	ARG ARG	165 165	11.169 11.512	17.760 18.971	8.990 9.415	1.00 22.12 1.00 22.71
	MOTA	1321	NHl	ARG	165	10.641	19.972	9.383	1.00 22.71
	ATOM ATOM	1322 1323	NH2 C	ARG	165 165	12.734	19.177	9.883	1.00 22.67
00	ATOM	1323	0	ARG ARG	165	6.068 5.655	15.546 14.396	7.076 7.207	1.00 30.34 1.00 31.07
80	ATOM	1325	N	ALA	166	5.575	16.381	6.171	1.00 30.71
	ATOM	1326	CA	ALA	166	4.507	15.945	5.287	1.00 30.26

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	MOTA	1327 CB ALA		3.891 17.146	4.567 1.00 31.74
	ATOM ATOM	1328 C ALA 1329 O ALA		5.051 14.946	4.276 1.00 28.73
_	ATOM	1330 N TRP	166 167	6.240 14.961 4.166 14.070	3.950 1.00 26.64 3.806 1.00 28.10
5	ATOM	1331 CA TRP	167	4.475 13.046	3.806 1.00 28.10 2.806 1.00 27.46
	MOTA	1332 CB TRP	167	5.309 13.631	1.650 1.00 28.13
	MOTA ATOM	1333 CG TRP 1334 CD2 TRP	167	4.811 14.960	1.098 1.00 32.39
	ATOM	1335 CE2 TRP	167 167	3.672 15.177 3.616 16.560	0.245 1.00 31.61 -0.035 1.00 32.63
10	ATOM	1336 CE3 TRP	167	2.697 14.336	-0.035 1.00 32.63 -0.307 1.00 31.53
	ATOM	1337 CD1 TRP	167	5.378 16.192	1.292 1.00 33.04
	ATOM	1338 NE1 TRP	167	4.666 17.155	0.614 1.00 33.34
	ATOM ATOM	1339 CZ2 TRP 1340 CZ3 TRP	167 167	2.620 17.123 1.702 14.899	-0.847 1.00 32.95
15	ATOM	1341 CH2 TRP	167	1.702 14.899 1.675 16.277	-1.121 1.00 31.83 -1.379 1.00 32.36
	ATOM	1342 C TRP	167	5.172 11.789	-1.379 1.00 32.36 3.327 1.00 27.06
	ATOM	1343 O TRP	167	5.413 10.863	2.550 1.00 27.23
	MOTA MOTA	1344 N LEU 1345 CA LEU	168 168	5.507 11.737	4.617 1.00 26.83
20	ATOM	1346 CB LEU	168	6.161 10.537 6.521 10.703	5.145 1.00 26.56 6.633 1.00 27.73
	ATOM	1347 CG LEU	168	7.684 11.644	6.633 1.00 27.73 7.009 1.00 26.59
	ATOM	1348 CD1 LEU	168	7.798 11.758	8.529 1.00 25.28
	MOTA ATOM	1349 CD2 LEU 1350 C LEU	168	8.982 11.124	6.417 1.00 25.28
25	ATOM	1350 C LEU 1351 O LEU	168 168	5.217 9.347 4.022 9.457	4.973 1.00 28.20
	ATOM	1352 N LEU	169	5.755 8.219	5.241 1.00 26.68 4.513 1.00 28.02
	ATOM	1353 CA LEU	169	4.954 7.016	4.307 1.00 28.10
	ATOM	1354 CB LEU	169	5.588 6.132	3.231 1.00 27.55
30	ATOM ATOM	1355 CG LEU 1356 CD1 LEU	169 169	5.571 6.687	1.802 1.00 29.51
	ATOM	1357 CD2 LEU	169	6.406 5.802 4.130 6.785	0.879 1.00 26.49 1.319 1.00 26.84
•	MOTA	1358 C LEU	169	4.785 6.216	5.593 1.00 29.45
	ATOM	1359 O LEU	169	3.754 5.582	5.800 1.00 30.01
35	ATOM ATOM	1360 N GLU 1361 CA GLU	170 170	5.801 6.237	6.452 1.00 29.04
-	ATOM	1362 CB GLU	170	5.736 5.518 6.684 4.315	7.721 1.00 29.15 7.706 1.00 29.47
	MOTA	1363 CG GLU	170	6.321 3.256	7.706 1.00 29.47 6.672 1.00 32.25
	ATOM	1364 CD GLU	170	7.296 2.095	6.659 1.00 32.48
40	MOTA MOTA	1365 OE1 GLU 1366 OE2 GLU	170 170	8.494 2.323	6.391 1.00 35.86
	ATOM	1367 C GLU	170	6.866 0.954 6.106 6.453	6.918 1.00 33.16 8.863 1.00 28.40
	MOTA	1368 O GLU	170	7.150 6.297	8.863 1.00 28.40 9.493 1.00 26.92
	MOTA	1369 N. PRO	171	5.241 7.440	9.148 1.00 29.50
45	ATOM ATOM	1370 CD PRO1. 1371 CA PRO	171 171	3.953 7.686	8.474 1.00 28.57
	MOTA	1372 CB PRO	171	5.467 8.416 4.238 9.320	10.217 1.00 29.67 10.125 1.00 30.97
	ATOM	1373 CG PRO	171	3.174 8.408	9.536 1.00 29.77
	ATOM ATOM	1374 C PRO 1375 O PRO	171	5.652 7.816	11.610 1.00 31.30
50	MOTA	1375 O PRO 1376 N ARG	171 172	6.520 8.259 4.838 6.815	12.371 1.00 28.88
	ATOM	1377 CA ARG	172	4.838 6.815 4.915 6.153	11.940 1.00 31.06 13.240 1.00 32.55
	ATOM	1378 CB ARG	172	3.916 4.992	13.299 1.00 36.17
	ATOM ATOM	1379 CG ARG	172	2.639 5.296	14.065 1.00 42.42
55	ATOM	1380 CD ARG 1381 NE ARG	172 172	2.802 4.986 3.861 5.774	15.561 1.00 49.54
	ATOM	1382 CZ ARG	172	3.861 5.774 4.305 5.573	16.202 1.00 53.35 17.443 1.00 55.25
	MOTA	1383 NH1 ARG	172	3.788 4.604	18.192 1.00 56.19
	ATOM ATOM	1384 NH2 ARG	172	5.268 6.342	17.941 1.00 56.24
60	ATOM	1385 C ARG 1386 O ARG	172 172	6.319 5.637 6.764 5.702	13.552 1.00 31.45
	ATOM	1387 N LYS	173	6.764 5.702 7.010 5.117	14.702 1.00 30.68 12.540 1.00 29.22
	ATOM	1388 CA LYS	173	8.363 4.615	12.743 1.00 29.66
	ATOM	1389 CB LYS	173	8.861 3.870	11.503 1.00 32.78
65	ATOM ATOM	1390 CG . LYS 1391 CD LYS	173 173	8.200 2.513 8.782 1.776	11.305 1.00 37.00
	ATOM	1392 CE LYS	173	8.782 1.776 8.072 0.449	10.116 1.00 39.09 9.888 1.00 41.03
	ATOM	1393 NZ LYS	173	8.678 -0.294	9.888 1.00 41.03 8.745 1.00 43.13
	ATOM	1394 C LYS	173	9.300 5.768	13.076 1.00 28.29
70	ATOM ATOM	1395 O LYS 1396 N VAL	173	10.207 5.625	13.894 1.00 26.75
, 0	ATOM	1396 N VAL 1397 CA VAL	174 174	9.082 6.913 9.903 8.085	12.441 1.00 26.90
	ATOM	1398 CB VAL	174	9.903 8.085 9.616 9.215	12.713 1.00 25.57 11.709 1.00 23.33
	ATOM	1399 CG1 VAL	174	10.401 10.474	12.096 1.00 20.63
<i>7</i> 5	ATOM	1400 CG2 VAL	174	9.999 8.758	10.303 1.00 22.21
, 5	ATOM ATOM	1401 C VAL 1402 O VAL	174	9.587 8.575	14.122 1.00 26.24
	ATOM	1402 U VAL 1403 N GLN	174 175	10.484 8.917 8.303 8.603	14.889 1.00 24.66
	MOTA	1404 CA GLN	175	7.869 9.040	14.458 1.00 27.11 15.779 1.00 28.66
80	ATOM	1405 CB GLN	175	6.339 8.967	15.878 1.00 31.02
ου	ATOM	1406 CG GLN	175	5.779 9.114	17.286 1.00 38.22
	MOTA	1407 CD GLN	175	4.257 9.212	17.301 1.00 42.67

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5	ATOM	1492	N	LEU	185	17.862	12.429	25.441	1.00 24.98
J	ATOM	1493 1494	CA	LEU	185	18.268	13.816	25.620	1.00 24.30
	MOTA MOTA	1494	CB CG	LEU	185 185	17.704	14.671	24.488	1.00 24.30
	ATOM	1496	CD:	LEU LEU	185	17.940	16.182	24.573	1.00 24.55
	ATOM	1497	CD		185	19.449 17.283	16.479	24.607	1.00 21.33
10	ATOM	1498	c c	LEU	185	17.821	16.860 14.392	23.367	1.00 22.54
	ATOM	1499	ŏ	LEU	185	18.537	15.178	26.957	1.00 24.99
	ATOM	1500	N	GLN	186	16.631	14.011	27.569 27.400	1.00 24.67
	ATOM	1501	CA	GLN	186	16.103	14.506	28.660	1.00 25.81 1.00 26.62
	ATOM	1502	СВ	GLN	186	14.694	13.966	28.876	1.00 20.02
15	ATOM	1503	CG	GLN	186	13.997	14.508	30.094	1.00 36.75
	ATOM	1504	CD	GLN	186	12.629	13.896	30.263	1.00 43.23
	ATOM	1505	OE	GLN	186	12.491	12.666	30.304	1.00 46.44
	MOTA	1506	NE	GLN	186	11.602	14.744	30.354	1.00 43.40
20	ATOM	1507	С	GLN	186	17.006	14.073	29.807	1.00 27.38
20	ATOM	1508	0	GLN	186	17.212	14.824	30.762	1.00 27.01
	ATOM	1509	N	HIS	187	17.544	12.860	29.715	1.00 27.90
	ATOM	1510	CA	HIS	187	18.433	12.356	30.756	1.00 27.79
	ATOM	1511	CB	HIS	187	18.610	10.846	30.604	1.00 28.15
25	ATOM	1512	CG	HIS	187	17.409	10.064	31.028	1.00 29.94
20	ATOM	1513		HIS	187	16.329	9.642	30.330	1.00 31.20
	ATOM ATOM	. 1514	ND1		187	17.185	9.695	32.337	1.00 32.49
	ATOM	1515 1516	CE1	HIS HIS	187	16.019	9.083	32.428	1.00 30.69
	ATOM	1517	C	HIS	187	15.478	9.038	31.225	1.00 32.71
30	ATOM	1518	õ	HIS	187 187	19.785 20.312	13.066	30.724	1.00 27.63
	ATOM	1519	N	VAL	188	20.312	13.450 13.251	31.771	1.00 25.57
	ATOM	1520	CA	VAL	188	21.623	13.932	29.526 29.371	1.00 27.19
	ATOM	1521	СВ	VAL	188	22.032	14.045	27.876	1.00 26.76 1.00 27.81
~=	ATOM	1522	CG1		188	23.281	14.923	27.734	1.00 27.81
35	ATOM	1523	CG2		188	22.283	12.657	27.301	1.00 26.52
	ATOM	1524	С	VAL	188	21.545	15.341	29.954	1.00 27.08
	ATOM	1525	0	VAL	188	22.460	15.801	30.639	1.00 27.95
	ATOM	1526	N	ILE	189	20.444	16.023	29.675	1.00 26.81
40	ATOM	1527	CA	ILE	189	20.243	17.382	30.156	1.00 28.56
40	ATOM	1528	CB	ILE	189	18.865	17.902	29.700	1.00 27.38
	ATOM	1529	CG2		189	18.428	19.099	30.549	1.00 27.87
	ATOM	1530	CG1		189	18.940	18.263	28.213	1.00 25.31
	ATOM ATOM	1531 1532	CD1		189	17.612	18.583	27.585	1.00 23.03
45	ATOM	1533	С 0	ILE	189	20.381	17.482	31.675	1.00 29.59
	ATOM	1534	N	GLN	189 190	20.810	18.504	32.205	1.00 28.17
	ATOM	1535	CA	GLN	190	20.025 20.130	16.413	32.374	1.00 31.73
	ATOM	1536	СВ	GLN	190	19.517	16.401 15.115	33.824 34.383	1.00 34.66
	ATOM	1537	CG	GLN	190	18.181	14.749	33.767	1.00 35.71 1.00 36.32
50	ATOM	1538	CD	GLN	190	17.525	13.575	34.469	1.00 36.32 1.00 37.87
	ATOM	1539	OE1	GLN	190	18.207	12.705	35.008	1.00 37.94
	ATOM	1540	NE2	GLN	190	16.195	13.537	34.453	1.00 37.69
	ATOM	1541	С	GLN	190	21.589	16.522	34.282	1.00 36.42
55	ATOM	1542	0	GLN	190	21.864	17.088	35.341	1.00 37.31
55	ATOM	1543	N	LYS.	191	22.522	15.995	33.491	1.00 36.35
	ATOM	1544	CA	LYS	191	23.944	16.060	33.849	1.00 38.86
	ATOM	1545	СВ	LYS	191	24.816	15.373	32.798	1.00 36.60
	MOTA	1546	CG	LYS	191	24.892	13.887	32.917	1.00 34.28
60	MOTA MOTA	1547 1548	CE	LYS	191	26.075	13.357	32.132	1.00 33.89
00	ATOM	1549	NZ	LYS LYS	191	25.937	13.646	30.650	1.00 32.20
	ATOM	1550	C	LYS	191 191	27.090	13.103	29.891	1.00 33.09
	ATOM	1551	ŏ	LYS	191	24.424	17.491	33.962	1.00 40.84
	ATOM	1552	N	ASN	192	25.233 23.928	17.835	34.822	1.00 40.86
65	ATOM	1553	CA	ASN	192	24.297	18.318 19.714	33.056	1.00 43.43
	ATOM	1554	CB	ASN	192	24.297		33.003	1.00 45.38
	ATOM	1555	CG	ASN	192	25.345	20.071	31.541	1.00 44.67
	ATOM	1556		ASN	192	26.513	18.985 18.751	30.817	1.00 44.92
	ATOM	1557	ND2		192	24.705	18.301	31.126 29.870	1.00 42.55
70	ATOM	1558	С	ASN	192	23.151	20.518	33.607	1.00 43.86
	ATOM	1559	ŏ	ASN	192	22.728	20.250	34.732	1.00 47.90 1.00 50.09
	ATOM	1560	N	HIS	193	22.653	21.490	32.859	1.00 50.09
	ATOM	1561	CA	HIS	193	21.548	22.351	33.281	1.00 48.81
	ATOM	1562	СВ	HIS	193	20.616	22.551	32.091	1.00 31.29
<i>7</i> 5	ATOM	1563	CG	HIS	193	21.321	22.468	30.777	1.00 49.88
	ATOM	1564		HIS	193	21.274	21.535	29.798	1.00 47.56
	ATOM	1565	ND1	HIS	193	22.270	23.387	30.387	1.00 47.61
	MOTA	1566		HIS	193	22.780	23.022	29.224	1.00 48.67
00	ATOM	1567		HIS	193	22.193	21.901	28.846	1.00 47.30
80	ATOM	1568	C	HIS	193	20.730	21.875	34.487	1.00 53.71
	ATOM	1569	0	HIS	193	19.715	21.195	34.328	1.00 53.57

	MOTA	1570	N	LEU	194		21.168	22.233	35.692	1 00 57 22
	ATOM	1571	CA	LEU	194		20.433	21.852	36.897	1.00 57.22 1.00 60.04
	ATOM	1572	СВ	LEU	194		21.288	22.076		
	ATOM	1573	CG	LEU	194		20.990	21.191	38.151	1.00 60.66
5	ATOM	1574		LEU	194		19.593	21.191	39.372 39.902	1.00 61.69
9		1575		LEU	194		21.127	19.716		1.00 61.58
	ATOM								38.987	1.00 60.81
	MOTA	1576	C	LEU	194		19.240	22.797	36.874	1.00 61.24
	MOTA	1577	0	LEU	194		19.397	23.968	36.530	1.00 61.98
10	MOTA	1578	N	ASP	195		18.059	22.304	37.242	1.00 62.55
10	MOTA	1579	CA	ASP	195		16.846	23.119	37.178	1.00 63.43
	MOTA	1580	СВ	ASP	195		17.019	24.440	37.937	1.00 66.10
	MOTA	1581	CG	ASP	195		16.716	24.303	39.424	1.00 67.60
	MOTA	1582	OD1	ASP	195		17.314	23.423	40.082	1.00 67.56
	MOTA	1583	OD2	ASP	195		15.875	25.076	39.934	1.00 68.82
15	MOTA	1584	С	ASP	195		16.696	23.351	35.681	1.00 62.91
	MOTA	1585	0	ASP	195		17.481	24.071	35.062	1.00 62.29
	ATOM	1586	N	ASP	196		15.680	22.739	35.095	1.00 62.38
	MOTA	1587	CA	ASP	196		15.525	22.819	33.661	1.00 61.54
	MOTA	1588	СВ	ASP	196		15.581	21.397	33.106	1.00 62.97
20	ATOM	1589	CG	ASP	196		14.499	20.508	33.693	1.00 63.92
	ATOM	1590	OD1	ASP	196		13.365	20.512	33.165	1.00 63.95
	ATOM	1591		ASP	196		14.777	19.817	34.697	1.00 64.35
	ATOM	1592	C	ASP	196		14.350	23.545	33.028	1.00 60.76
	ATOM	1593	ō	ASP	196		14.171	24.758	33.190	1.00 59.34
25	ATOM	1594	N	GLU	197		13.572	22.747	32.298	1.00 58.84
	ATOM	1595	CA	GLU	197		12.429	23.157	31.494	1.00 57.17
	ATOM	1596	СВ	GLU	197		11.960	24.576	31.830	1.00 59.78
	ATOM	1597	CG	GLU	197		10.901	25.109	30.876	1.00 63.41
	ATOM	1598	CD	GLU	197		10.666	26.601	31.023	1.00 66.17
30	MOTA	1599		GLU	197		9.831	27.144	30.268	
50		1600		GLU	197		11.313	27.231	31.888	1.00 67.86
	ATOM									1.00 68.19
	ATOM	1601	C	GLU	197		13.138	23.163	30.147	1.00 53.54
	ATOM	1602	0	GLU	197		12.537	23.364	29.092	1.00 54.00
35	MOTA	1603	N	THR	198		14.446	22.924	30.229	1.00 48.95
55	ATOM	1604	CA	THR	198		15.345	22.910	29.088	1.00 43.99
	ATOM	1605	CB	THR	198		16.731	22.376	29.499	1.00 43.60
	MOTA	1606		THR	198		17.251	23.185	30.559	1.00 42.61
	ATOM	1607		THR	198		17.699	22.422	28.318	1.00 43.36
40	ATOM	1608	С	THR	198		14.842	22.125	27.889	1.00 39.98
<b>40</b>	MOTA	1609	0	THR	198		14.772	22.665	26.790	1.00 39.06
	MOTA	1610	N	LEU	199		14.497	20.857	28.084	1.00 37.03
	MOTA	1611	CA	LEU	199		14.009	20.057	26.966	1.00 35.00
	ATOM	1612	CB	LEU	199		13.650	18.639	27.414	1.00 34.87
15	ATOM	1613	CG	LEU	199		13.972	17.518	26.418	1.00 34.97
45	MOTA	1614		LEU	199		13.114	16.299	26.728	1.00 34.01
	ATOM	1615		LEU	199		13.729	17.980	25.004	1.00 33.06
	ATOM	1616	C.	LEU	199		12. <b>7</b> 74	20.725	26.362	1.00 33.27
	ATOM	1617	0	LEU	199		12.668	20.860	25.148	1.00 31.34
<b>~</b> 0	MOTA	1618	N	ALA	200		11.849	21.147	27.219	1.00 32.76
50	MOTA	1619	CA	ALA	200		10.625	21.804	26.763	1.00 33.19
	MOTA	1620	СВ	ALA	200		9.706	22.120	27.963	1.00 32.22
	ATOM	1621	С	ALA	200		10.956	23.084	26.002	1.00 32.43
	MOTA	1622	0	ALA	200		10.341	23.380	24.977	1.00 31.79
	ATOM	1623	N	LYS	201		11.931	23.841	26.497	1.00 32.28
55	ATOM	1624	CA	LYS	201		12.327	25.084	25.838	1.00 32.01
	MOTA	1625	СВ	LYS	201		13.342	25.854	26.682	1.00 35.09
	ATOM	1626	CG	LYS	201		12.853	26.322	28.036	1.00 36.56
	ATOM	1627	CĐ	LYS	201		13.903	27.242	28.652	1.00 40.79
	ATOM	1628	CE	LYS	201		13.616	27.553	30.107	1.00 43.94
60	ATOM	1629	NZ	LYS	201		14.677	28.430	30.671	1.00 47.03
	MOTA	1630	С	LYS	201		12.946	24.787	24.480	1.00 30.91
	ATOM	1631	0	LYS	201		12,775	25.552	23.531	1.00 30.11
	ATOM	1632	N	LEU	202		13.683	23.683	24.391	1.00 30.46
	ATOM	1633	CA	LEU	202		14.307	23.297	23.129	1.00 29.29
65	ATOM	1634	СВ	LEU	202		15.258	22.117	23.331	1.00 28.23
-	ATOM	1635	CG	LEU	202		16.633	22.426	23.923	1.00 29.50
	MOTA	1636		LEU	202		17.429	21.126	24.055	1.00 27.57
	ATOM	1637			202		17.367	23.417		
				LEU	202		13.224		23.022	1.00 27.80
70	ATOM	1638	C	LEU				22.906	22.138	1.00 28.85
, 0	ATOM	1639	0	LEU	202		13.181	23.399	21.011	1.00 30.02
	ATOM	1640	N	ILE	203		12.348	22.011	22.567	1.00 28.20
	ATOM	1641	CA	ILE	203		11.261	21.552	21.722	1.00 29.72
	ATOM	1642	CB	ILE	203		10.370	20.553	22.498	1.00 30.66
75	ATOM	1643		ILE	203		9.101	20.248	21.709	1.00 31.62
<i>7</i> 5	MOTA	1644		ILE	203		11.165	19.271	22.774	1.00 33.22
	ATOM	1645		ILE	203		10.477	18.296	23.714	1.00 33.21
	ATOM	1646	С	ILE	203		10.415	22.729	21.217	1.00 28.90
	MOTA	1647	0	ILE	203		9.962	22.734	20.073	1.00 26.56
00	ATOM	1648	N	ALA	204		10.228	23.733	22.070	1.00 28.33
80	ATOM	1649	CA	ALA	204		9.434	24.904	21.716	1.00 28.52
	ATOM	1650	CB	ALA	204	•	9.188	25.761	22.948	1.00 29.61

	ATOM	1651	С	ALA	204	10.0	176	25 754	20 620	1 00 00 05
	ATOM	1652	ō	ALA	204	9.4		25.754 26.622	20.629	
	ATOM	1653	N	LYS	205	11.3		25.520	20.054	1.00 28.72
_	ATOM	1654	CA	LYS	205	12.0		26.293	19.326	1.00 27.27 1.00 27.82
5	ATOM	1655	CB	LYS	205	13.5		26.443	19.674	1.00 28.06
	ATOM	1656	CG	LYS	205	13.7		27.246	20.941	1.00 31.35
	ATOM	1657	CD	LYS	205	15.2		27.343	21.249	1.00 32.78
•	ATOM	1658	CE	LYS	205	15.5		27.938	22.624	1.00 36.42
40	ATOM	1659	NZ	LYS	205	14.8		29.262	22.784	1.00 40.34
10	ATOM	1660	С	LYS	205	11.8	94	25.657	17.945	1.00 27.11
	MOTA	1661	0	LYS	205	12.2	05	26.284	16.938	1.00 28.06
	ATOM	1662	N	ILE	206	11.4	17	24.418	17.897	1.00 27.34
	MOTA	1663	CA	ILE	206	11.2	56	23.725	16.621	1.00 28.94
15	ATOM	1664	CB	ILE	206	10.4	53	22.417	16.794	1.00 29.50
15	MOTA	1665		ILE	206	10.1	59	21.801	15.429	1.00 31.00
	ATOM	1666	CG1		206	11.2		21.447	17.703	1.00 28.15
	ATOM	1667		ILE	206	12.4		20.830	17.088	1.00 28.61
	ATOM	1668	C	ILE	206	10.5		24.590	15.559	1.00 29.28
20	ATOM	1669	0	ILE	206	11.0		24.783	14.462	1.00 30.10
20	ATOM	1670	N	PRO	207	9.3		25.125	15.869	1.00 30.04
	ATOM	1671	CD	PRO	207	8.5		24.973	17.089	1.00 29.62
	ATOM ATOM	1672 1673	CA	PRO	207	8.6		25.957	14.877	1.00 30.42
	ATOM	1674	CB CG	PRO PRO	207 207	7.3		26.337	15.582	1.00 31.19
25	ATOM	1675	C	PRO	207	7.6		26.204	17.041	1.00 33.14
	ATOM	1676	ŏ	PRO	207	9.4		27.165	14.417	1.00 29.62
	ATOM	1677	N	THR	208	9.3		27.616	13.281	1.00 29.83
	ATOM	1678	CA	THR	208	10.3		27.675	15.290	1.00 26.85
	ATOM	1679	CB	THR	208	11.1 11.8		28.819	14.935	1.00 28.12
30	ATOM	1680		THR	208	10.8		29.396 29.918	16.159	1.00 29.03
	ATOM	1681	CG2		208	12.8		30.506	17.052 15.751	1.00 31.90
	ATOM	1682	c	THR	208	12.2		28.407	13.751	1.00 29.68
	ATOM	1683	ō	THR	208	12.4		29.113	12.944	1.00 28.22
~=	ATOM	1684	N	ILE	209	12.8		27.252	14.142	1.00 28.12 1.00 26.44
35	ATOM	1685	CA	ILE	209	13.8		26.746	13.240	1.00 25.22
	ATOM	1686	CB	ILE	209	14.3		25.383	13.732	1.00 23.83
	ATOM	1687	CG2	ILE	209	15.30	80	24.776	12.693	1.00 23.71
	ATOM	1688	CG1		209	15.0	79	25.568	15.081	1.00 21.30
40	ATOM	1689	CD1		209	15.64	44	24.294	15.685	1.00 21.88
<b>40</b>	ATOM	1690	Ç	ILE	209	13.29		26.602	11.842	1.00 23.64
	ATOM	1691	0	ILE	209	13.88		26.965	10.847	1.00 24.10
	ATOM	1692	N	THR	210	12.03		26.083	11.781	1.00 23.76
	ATOM	1693	CA	THR	210	11.33		25.888	10.520	1.00 21.79
45	MOTA MOTA	··1694	CB	THR	210	10.04		25.064	10.737	1.00 22.51
10	ATOM	1695 1696	CG2	THR	210	10.39		23.748	11.173	1.00 21.60
	ATOM	1697	C	THR THR	210 210	9.24		24.958	9.448	1.00 24.33
	ATOM	1698	ŏ	THR	210	10.97 11.03		27.202	9.825	1.00 22.08
	ATOM	1699	N	ALA	211	10.60		27.289 28.220	8.603	1.00 22.39
- 50	ATOM	1700	CA	ALA	211	10.23		29.526	10.600 10.037	1.00 22.88
	ATOM	1701	СВ	ALA	211	9.67		30.435	11.127	1.00 22.29
	ATOM	1702	С	ALA	211	11.45		30.186	9.384	1.00 23.28 1.00 23.47
	ATOM	1703	0	ALA	211	11.33		30.822	8.335	1.00 23.25
~ <del>~</del> ~	ATOM	1704	N	VAL	212	12.61		30.045	10.006	1.00 22.80
55	ATOM	1705	CA	VAL	212	13.82		30.627	9.433	1.00 23.37
	MOTA	1706	CB	VAL	212	15.04		30.433	10.353	1.00 23.62
	ATOM	1707		VAL	212	16.29	8	30.998	9.684	1.00 22.67
	ATOM	1708		VAL	212	14.81		31.125	11.682	1.00 24.14
60	ATOM	1709	C	VAL	212	14.11		2 <b>9</b> .970	8.088	1.00 23.99
UU	ATOM	1710	0	VAL	212	14.40		30.649	7.106	1.00 25.86
	ATOM	1711	N	CYS	213	14.01		28.645	8.041	1.00 23.57
	ATOM	1712	CA	CYS	213	14.28		27.910	6.814	1.00 25.76
	ATOM	1713	CB	CYS	213	14.40		26.411	7.123	1.00 25.45
65	ATOM ATOM	1714	SG	CYS	213	15.84		26.040	8.202	1.00 29.19
00	ATOM	1715 1716	C	CYS	213	13.25		28.167	5.704	1.00 27.48
	ATOM	1717	0	CYS	213	13.61		28.194	4.521	1.00 26.56
	ATOM	1718	N CA	ASN	214	11.99		28.358	6.063	1.00 28.96
	ATOM	1719	CB	ASN ASN	214	10.99		28.640	5.031	1.00 30.22
<i>7</i> 0 ·	ATOM	1720	CG	ASN	214 214	9.57 9.12		28.612	5.592	1.00 32.61
. •	ATOM	1721	ODI		214			27218	5.987	1.00 34.72
	ATOM	1722	ND2		214	9.48 8.33		26.237	5.337	1.00 35.64
	ATOM	1723	C	ASN	214	11.29		27.128	7.043	1.00 36.05
	MOTA	1724	õ	ASN	214	11.16		30.021	4.473	1.00 29.75
<i>7</i> 5	ATOM	1725	N	LEU	215	11.71		30.260 30.930	3.275	1.00 30.40
	ATOM	1726		LEU	215	12.03	_	32.278	5.348	1.00 28.89
	ATOM	1727		LEU	215	12.41		33.151	4.909 6.104	1.00 27.73
	ATOM	1728		LEU	215	12.53		34.649	5.816	1.00 26.66 1.00 28.15
00	ATOM	1729	CD1		215	11.29		35.147	5.064	1.00 28.15
80	ATOM	1730	CD2		215	12.69	9	35.393	7.124	1.00 29.37
	ATOM	1731		LEU	215	13.17		32.197	3.904	1.00 27.61

	ATOM	1732	O LEU	215	13.206	32.939	2.918	1.00 27.88
	ATOM	1733	N HIS	216	14.119	31.284	4.150	1.00 26.67
	ATOM	1734	CA HIS	216	15.246	31.081	3.244	1.00 25.98
	ATOM	1735	CB HIS	216	16.177	29.982	3.777	1.00 26.15
5	ATOM	1736	CG HIS	216	17.116	29.420	2.748	1.00 25.88
_	ATOM	1737	CD2 HIS	216	18.361	29.799	2.372	1.00 25.25
	ATOM	1738	ND1 HIS	216	16.785	28.351	1.942	
	ATOM	1739	CE1 HIS	216	17.784	28.098		1.00 27.09
	ATOM	1740	NE2 HIS	216	18.753		1.115	1.00 26.92
10		1741				28.964	1.355	1.00 24.89
10	MOTA		C HIS	216	14.692	30.674	1.884	1.00 26.04
	ATOM	1742	O HIS	216	15.052	31.247	0.860	1.00 26.79
	ATOM	1743	N GLY	217	13.810	29.681	1.885	1.00 26.73
	MOTA	1744	CA GLY	217	13.220	29.223	0.641	1.00 28.62
1 -	ATOM	1745	C GLY	217	12.537	30.359	-0.096	1.00 30.50
15	ATOM	1746	O GLY	217	12.648	30.471	-1.314	1.00 30.23
	MOTA	1747	N GLU	218	11.829	31.209	0.644	1.00 33.00
	ATOM	1748	CA GLU	218	11.128	32.344	0.050	1.00 34.40
	ATOM	1749	CB GLU	218	10.279	33.050	1.110	1.00 37.30
	ATOM	1750	CG GLU	218	9.078	32.243	1.568	1.00 43.62
20	ATOM	1751	CD GLU	218	8.375	32.862	2.765	1.00 48.13
	ATOM	1752	OE1 GLU	218	8.082	34.077	2.718	1.00 50.14
	ATOM	1753	OE2 GLU	218	8.108	32.131	3.750	
	ATOM	1754	C GLU	218	12.092	33.338		1.00 50.72
	ATOM	1755	O GLU	218	11.906	33.735	-0.590	1.00 33.43
25	ATOM	1756		219			-1.735	1.00 33.17
20	ATOM				13.120	33.742	0.151	1.00 33.47
		1757 1758	CA LYS	219	14.100	34.686	-0.368	1.00 33.64
	ATOM		CB LYS	219	15.188	34.972	0.677	1.00 33.37
	ATOM	1759	CG LYS	219	14.707	35.722	1.911	1.00 34.09
30	ATOM	1760	CD LYS	219	14.125	37.076	1.537	1.00 35.69
30	MOTA	1761	CE LYS	219	13.682	37.852	2.765	1.00 39.13
	MOTA	1762	NZ LYS	219	13.047	39.158	2.399	1.00 40.00
	MOTA	1763	C LYS	219	14.745	34.118	-1.625	1.00 35.52
	MOTA	1764	O LYS	219	15.051	34.847	-2.573	1.00 34.96
0.5	MOTA	1765	N LEU	220	14.950	32.807	-1.626	1.00 35.22
35	MOTA	1766	CA LEU	220	15.566	32.138	-2.759	1.00 36.55
	MOTA	1767	CB LEU	220	15.877	30.690	-2.389	1.00 37.39
	MOTA	1768	CG LEU	220	16.647	29.830	-3.383	1.00 38.60
	ATOM	1769	CD1 LEU	220	17.945	30.519	-3.792	1.00 38,29
	ATOM	1770	CD2 LEU	220	16.936	28.489	-2.729	1.00 39.42
<b>4</b> 0	ATOM	1771	C LEU	220	14.652	32.186	-3.979	1.00 37.19
	ATOM	1772	O LEU	220	15.102	32.465	-5.086	1.00 37.42
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	ATOM	1774	CA GLN	221	12.409	31.930	-4.870	1.00 39.61
	ATOM	1775	CB →GLN	221	11.002	31.632	-4.350	
45	ATOM	1776	CG GLN	221	10.849	30.214	-3.829	1.00 43.16
	ATOM	1777	CD GLN	221	11.363	29.177		1.00 47.61
	ATOM	1778	OE1 GLN	221	10.772	28.966	-4.820	1.00 51.15
	ATOM	1779	NE2 GLN	221	12.480	28.534	-5.881	1.00 52.70
_	ATOM	1780	C GLN	221			-4.479	1.00 51.82
50	ATOM	1781			12.420	33.261	-5.607	1.00 38.21
00	ATOM	1782		221	12.365	33.296	-6.835	1.00 37.75
			N VAL	222	12.497	34.354	-4.857	1.00 36.97
	ATOM	1783	CA VAL	222	12.529	35.676	-5.467	1.00 37.21
	ATOM	1784	CB VAL	222	12.377	36.795	-4.411	1.00 36.85
55	MOTA	1785	CG1 VAL	222	12.444	38.154	-5.086	1.00 37.24
55	MOTA	1786	CG2.VAL	222	11.050	36.645	-3.678	1.00 37.77
	MOTA	1787	C VAL	222	13.846	35.867	-6.217	1.00 37.47
	ATOM	1788	O VAL	222	13.869	36.424	-7.316	1.00 37.13
	MOTA	1789	N PHE	223	14.943	35.400	-5.624	1.00 37.83
<b>60</b>	ATOM	1790	CA PHE	223	16.248	35.521	-6.268	1.00 39.20
60	ATOM	1791	CB PHE	223	17.349	34.906	-5.392	1.00 37.95
	MOTA	1792	CG PHE	223	18.731	35.023	~5.984	1.00 39.28
	ATOM	1793	CD1 PHE	223	19.405	36.238	-5.975	1.00 39.67
	MOTA	1794	CD2 PHE	223	19.339	33.927	-6.589	1.00 39.69
	MOTA	1795	CE1 PHE	223	20.666	36.362	-6.565	1.00 41.73
65	ATOM	1796	CE2 PHE	223	20.600	34.042	-7.180	1.00 40.32
	ATOM	1797	CZ PHE	223	21.262	35.263	-7.168	1.00 39.45
	ATOM	1798	C PHE	223	16.201	34.789	-7.612	1.00 40.64
	ATOM	1799	O PHE	223	16.767	35.249		
	ATOM	1800		224			-8.603	1.00 40.48
70			N LYS		15.520	33.647	-7.634	1.00 42.33
, 0	MOTA	1801	CA LYS	224	15.399	32.857	-8.851	1.00 45.23
	MOTA	1802	CB LYS	224	14.629	31.560	-8.571	1.00 47.13
	ATOM	1803	CG LYS	224	14.588	30.593	-9.749	1.00 50.45
	ATOM	1804	CD LYS	224	13.866	29.303	-9.383	1.00 52.28
75	ATOM	1805	CE LYS	224	13.785		-10.572	1.00 54.02
<i>7</i> 5	ATOM	1806	NZ LYS	224	13.051		-10.246	1.00 54.04
	ATOM	1807	C LYS	224	14.688	33.677	-9.925	1.00 45.85
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00	ATOM	1810	CA GLN	225	13.020	35.378	-10.448	1.00 48.45
80	ATOM	1811	CB GLN	225	11.936	36.196	-9.732	1.00 49.96
	ATOM	1812	CG GLN	225	10.784	35.397	-9.136	1.00 51.68
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5	ATOM	1897	O PHE		24.744	25.154	-8.687	1.00 29.90
9	MOTA MOTA	1898 1899	N PRO		25.259 25.543	25.251 25.924	-6.498	1.00 29.01
	ATOM	1900	-CA PRO		25.586	23.825	-5.220 -6.408	1.00 27.51 1.00 28.71
	MOTA	1901	CB PRO		25.967	23.652	-4.941	1.00 27.24
10	ATOM	1902	CG PRO		26.543	24.992	-4.598	1.00 28.61
10	ATOM ATOM	1903	C PRO		24.372	22.985	-6.788	1.00 29.15
	ATOM	1904 1905	O PRO		23.257 24.573	23.245	-6.336 -7.630	1.00 27.23
	ATOM	1906	CD PRO		25.811	21.603	-8.341	1.00 29.03 1.00 28.29
	MOTA	1907	CA PRO		23.460	21.113	-8.047	1.00 29.54
15	MOTA	1908	CB PRO		24.166	19.971	-8.765	1.00 29.15
	ATOM	1909	CG PRO		25.285	20.697	-9.457	1.00 30.03
	ATOM ATOM	1910 1911	C PRO		22.561 21.334	20.642 20.703	-6.898 -7.011	1.00 30.20
	ATOM	1912	N LEU		23.159	20.193	-5.795	1.00 28.77 1.00 29.38
20	ATOM	1913	CA LEU		22.371	19.720	-4.652	1.00 29.57
	ATOM	1914	CB LEU		23.280	19.148	-3.558	1.00 28.08
	ATOM	1915 1916	CG LEU		22.562	18.712	-2.271	1.00 27.84
	ATOM ATOM	1917	CD1 LEU		21.542 23.573	17.633 18.196	-2.597 -1.250	1.00 28.16
25	MOTA	1918	C LEU		21.504	20.828	-4.060	1.00 25.13 1.00 31.04
	MOTA	1919	O LEU		20.385	20.579	~3.608	1.00 31.07
	MOTA	1920	N TYR		22.022	22.051	-4.062	1.00 30.34
	ATOM	1921	CA TYR		21.290	23.189		1.00 31.47
30	ATOM ATOM	1922 1923	CB TYR		22.196 21.607	24.419 25.640	-3.509	1.00 30.35
00	ATOM	1924	CD1 TYR		20.775	26.513	-2.836 -3.535	1.00 29.41 1.00 30.76
	MOTA	1925	CE1 TYR		20.284	27.672	-2.934	1.00 30.78
	MOTA	1926	CD2 TYR		21.926	25.950	-1.514	1.00 28.97
35	ATOM	1927	CE2 TYR		21.442	27.101	-0.904	1.00 30.43
33	MOTA MOTA	1928 1929	CZ TYR OH TYR		20.625 20.177	27.960	-1.624	1.00 30.74
	MOTA	1930	C TYR	239	20.177	29.117 23.442	-1.037 -4.384	1.00 35.16 1.00 33.26
	ATOM	1931	O TYR		18.969	23.714	-3.870	1.00 33.26
40	MOTA	1932	N LYS	240	20.223	23.348	-5.699	1.00 33.87
40	ATOM	1933	CA LYS	240	19.100	23.546	-6.605	1.00 35.74
	MOTA MOTA	1934 1935	CB LYS	240	19.580	23.506	-8.058	1.00 37.63
	ATOM	1936	CG LYS	240 240	18.468 19.026	23.659 23.682	-9.083 -10.503	1.00 43.97 1.00 47.75
	ATOM	1937	CE LYS	240	17.906	23.676	-11.535	1.00 51.07
45	ATOM	1938	NZ LYS	240	18.426	23.651	-12.941	1.00 52.39
	MOTA	1939	C LYS	240	18.059	22.447	-6.370	1.00 35.10
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	ATOM	1947	OE1 GLU OE2 GLU	241 241	19.105 18.629	15.919 15.569	-6.792 -4.687	1.00 35.20
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65	ATOM	1957 1958	O LEU	242	14.755	21.721	-1.597	1.00 34.72
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70	MOTA	1963	CD2 PHE	243	16.309	24.446	0.277	1.00 34.27
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	MOTA MOTA	1966	CE2 PHE	243 243	17.051 18.442	23.992 23.941		1.00 36.44
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25	ATOM	2079	OH2 WAT	812	23.647	26.541	23.470	1.00 28.06
25	MOTA	2080	OH2 WAT	813	14.409	33.457	14.799	1.00 33.72
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30	ATOM	2085	OH2 WAT	818	3.298	4.825	10.176	1.00 23.53
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	ATOM	2093	OH2 WAT	835	3.146	11.579	6.786	
	ATOM	2094	OH2 WAT	836	8.412	22.351	12.154	1.00 34.28
40	ATOM	2095	OH2 WAT	837	14.427	24.078		1.00 37.30
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#### References

- Becker-André, M., André E., and DeLamarter, J. F. (1993) Identification of nuclear receptor mRNAs by RT-PCR amplification of conserved zinc-finger motif sequences. Biochem. Biophys. Res. Commun. 194, 1371-1379.
- Brünger, A.T. et al. Crystallography & NMR system: A new software suite for macromolecular structure determination. Acta Crystallogr. A47, 110-119, (1998).
  - Hirose, T., Smith, R. J., and Jetten, A. M. (1994) RORg: the third member of ROR/RZR orphan receptor subfamily that is highly expressed in skeletal muscle. Biochem. Biophys. Res. Commun. 205, 1976-1983.
- Jones, T. A., Zou, J. Y., Cowan, S. W. et Kjeldgaard, M. (1991) Improved methods for building protein models in electron density maps and the location of errors in theses models. Acta crystallogr. A47, 110-119
- 25 Kurebayashi S, and Hirose T. (1998) Novel orphan receptor: ROR gamma expressed during adipocyte differenciation. Nippon Rinsho, 56, 1729-1733.
- Lau P., Bailey P., Dowhan D. H., Muscat G.E. (1999) Exogenous expression of a dominant negative RORalpha1 vector in muscle cells impairs differenciation: RORalpha1 directly interacts with p300 and myoD. Nucleic Acids Research, 27, 411-420.
  - Koibuchi N., and Chin W., (1998) RORα gene expression in the perinatal rat cerebellum: ontogeny and thyroid hormone regulation. Endocrinology 139, 2335-2341.
  - Matysiak-Scholze U., and Nehls M. (1997) The structural integrity of RORα isoforms is mutated in *staggerer* mice: cerebellar coexpression of RORα1 and RORα4. Genomics, 43, 78-84.
- Navaza, J. (1994) AMoRe: an automated package for molecular replacement. Acta Crystallog. A50, 157-163.
- Nolte, R. T., Wisely G.B., Westin B., Cobbs J. E., Lambert M. H., Kurokawa R./, Rosenfeld M. G., Willson T., Glass C. K., and Millburn M. V. (1998) Ligand binding and co-activator assembly of the peroxisome proliferator-activated receptor-γ.
  - Otwinowski, Z., and Minor, W. (1997) Processing of X-ray diffraction data collected in oscillation mode. Methods Enzymol. 276, 307-326.
- Perrakis, A., Morris, R., and Lamzin V. S. (1999) Automated protein model building combined with iterative structure refinement. Nature Struct. Biol. 6, 458-463.
- Renaud, J-P, Rochel N., Ruff M., Vivat V., Chambon P., Gronemeyer H., and Moras D. (1995) Crystal structure of the RAR-γ ligand-binding domain bound to all-trans retinoic acid. Nature, 378, 681-689.

35

Rochel N., Wurtz J. M., Mitschler A., Klaholz B, and D. Moras. (2000) The crystal structure of the nuclear receptor for vitamin D bound to its natural ligand. Mol. Cell 5, 173-179.

5 Sirlin, J. L. (1956) Vacillans, a neurological mutant in the house mouse linked with brown. J. Genet., 54, 42-48.

BNSDOCID: <WO\_\_03000732A2\_I\_>

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### **CLAIMS**

- 1. Polypeptides derived from the retinoic acid-related orphan receptor (ROR) in mammals, characterized in that they are delimited in their N-terminal extremity by an amino-acid located between positions 1 to 209 of the rat, human, or murine ROR $\beta$ ,  $\alpha$ , or  $\gamma$ , as represented on figure 3, or by an amino-acid located at corresponding positions in nuclear receptor ROR of other subtypes than  $\alpha$ ,  $\beta$  and  $\gamma$ , and/or of other mammals, and in their C-terminal extremity by an amino-acid located between positions 450 to 452 of the rat, human, or murine ROR $\beta$ ,  $\alpha$ , or  $\gamma$ , as represented on figure 3, or by an amino-acid located at corresponding positions in nuclear receptor ROR of other subtypes than  $\alpha$ ,  $\beta$  and  $\gamma$ , and/or of other mammals.
- 2. Polypeptides according to claim 1, characterized in that at least the approximately 100 to 200 first amino-acids of the N-terminal part of the sequence of said receptor is deleted.
- 3. Polypeptides according to claim 1 or 2, derived from the nuclear receptor ROR, wherein the binding properties of the ligand-binding domain, or LBD, of said receptor, are maintained.
- 4. Polypeptides derived from the nuclear receptor RORβ, of mammals, such as human or rat, these derived polypeptides comprising a polypeptide as defined in claims 1 to 3, such as the polypeptides delimited by the amino-acids located in positions 201 to 459 of the sequences of rat or human RORβ represented on figure 3, said polypeptides being characterized in that at least one of the cysteine in position 454 or in position 458 of the amino-acid sequence of said nuclear receptor RORβ, as represented on figure 3, is deleted or substituted by another amino-acid, natural or not, such as alanine or serine.
- 5. Polypeptides according to any of claims 1 to 3, characterized in that they correspond to the fragments of mammals ROR, and more particularly of rat, human, or murine RORβ, α, or γ, delimited in their N-terminal extremity by the amino acid located in one of the positions 201 to 209 of the ROR sequences represented on figure 3, and in their C-terminal extremity by the amino acid located in one of the positions 451 or 452, of the ROR sequences represented on figure 3.
  - 6. Polypeptides according to any of claims 1 to 5, as defined above, chosen among: the fragment delimited by the amino acids located in positions 209 to 452 of:
  - the sequence of the rat ROR $\beta$  represented on figure 3, and corresponding to SEQ ID NO : 2,
  - . the sequence of the human ROR $\beta$  represented on figure 3, and corresponding to SEQ ID NO : 3,
  - . the sequence of the human ROR $\gamma$  represented on figure 3, and corresponding to SEQ ID NO : 4,
- . the sequence of the murine RORγ represented on figure 3, and corresponding to SEQ ID NO: 5,
  - . the sequence of the human ROR  $\alpha$  represented on figure 3, and corresponding to SEQ ID NO : 6,
- . the sequence of the murine ROR $\alpha$  represented on figure 3, and corresponding to SEQ ID NO : 7,
  - the fragment delimited by the amino acids located in positions 208 to 452 of:
  - . the sequence of the rat ROR $\beta$  represented on figure 3, and corresponding to SEQ ID NO : 8,
- . the sequence of the human ROR $\beta$  represented on figure 3, and corresponding to SEQ ID NO : 9,
  - . the sequence of the human RORγ represented on figure 3, and corresponding to SEQ ID NO: 10,

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(in the second

- . the sequence of the murine ROR $\gamma$  represented on figure 3, and corresponding to SEQ ID NO : 11,
- . the sequence of the human ROR $\alpha$  represented on figure 3, and corresponding to SEQ ID NO : 12,
- . the sequence of the murine RORα represented on figure 3, and corresponding to SEQ ID NO: 13,
  - the fragment delimited by the amino acids located in positions 208 to 451 of:
- . the sequence of the rat ROR $\beta$  represented on figure 3, and corresponding to SEQ ID NO : 14,
- 10 . the sequence of the human ROR $\beta$  represented on figure 3, and corresponding to SEQ ID NO : 15,
  - . the sequence of the human RORγ represented on figure 3, and corresponding to SEQ ID NO: 16,
- . the sequence of the murine RORγ represented on figure 3, and corresponding to SEQ ID NO: 17,
  - . the sequence of the human RORα represented on figure 3, and corresponding to SEQ ID NO: 18.
  - . the sequence of the murine ROR $\alpha$  represented on figure 3, and corresponding to SEQ ID NO : 19,
- the fragment delimited by the amino acids located in positions 209 to 451 of:
  the sequence of the rat RORβ represented on figure 3, and corresponding to SEO ID NO: 20.
  - the sequence of the human ROR $\beta$  represented on figure 3, and corresponding to SEO ID NO : 21.
- 25 . the sequence of the human RORγ represented on figure 3, and corresponding to SEQ ID NO: 22,
  - . the sequence of the murine RORγ represented on figure 3, and corresponding to SEQ ID NO: 23,
- . the sequence of the human RORα represented on figure 3, and corresponding to SEQ ID NO: 24,
  - . the sequence of the murine ROR $\alpha$  represented on figure 3, and corresponding to SEQ ID NO : 25,
    - the fragment delimited by the amino acids located in positions 201 to 451 of:
- the sequence of the rat RORβ represented on figure 3, and corresponding to SEQ ID NO: 26,
  - . the sequence of the human ROR $\beta$  represented on figure 3, and corresponding to SEQ ID NO : 27,
  - . the sequence of the human ROR $\gamma$  represented on figure 3, and corresponding to SEQ ID NO : 28,
- . the sequence of the murine RORγ represented on figure 3, and corresponding to SEQ ID NO: 29,
  - . the sequence of the human RORα represented on figure 3, and corresponding to SEQ ID NO: 30,
- . the sequence of the murine RORα represented on figure 3, and corresponding to SEQ ID NO: 31,
  - the fragment delimited by the amino acids located in positions 201 to 452 of:
  - the sequence of the rat ROR $\beta$  represented on figure 3, and corresponding to SEQ ID NO : 32,
- . the sequence of the human ROR $\beta$  represented on figure 3, and corresponding to SEQ ID NO : 33,
  - . the sequence of the human RORγ represented on figure 3, and corresponding to SEQ ID NO: 34,
  - . the sequence of the murine RORy represented on figure 3, and corresponding to SEQ ID NO: 35,
- 55 . the sequence of the human RORα represented on figure 3, and corresponding to SEQ ID NO: 36,

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9(3)

the sequence of the murine RORa represented on figure 3, and corresponding to SEQ ID NO: 37.

- 7. Polypeptides according to any one of claims 1 to 6, characterized by the following characteristics:
- they have the properties of binding a ligand and of transactivation of the LBD of the receptor ROR,

- they are soluble in aqueous solvants,

- they are crystallisable in aqueous solvents, especially by the hanging drop vapour

diffusion method, more particularly at approximately 4°C

or polypeptides or peptide sequences derived of those above mentioned, for example by suppression, addition or substitution of one or several amino acids, these polypeptides or peptide sequences having the characterisitics above mentioned.

15 8. Molecular complexes comprising a polypeptide according to any one of claims 1 to 7, said polypeptide being in association with:

- a ROR-LBD ligand which is an agonist, such as stearic acid, or an antagonist of the

ROR-LBD, such as retinoic acid,

- and/or with a co-peptide having a sequence of approximately 15-20 amino-acids and comprising the co-activator motif LXXLL or a co-repressor motif (I/L)XX(V/I)I or 20 LXX(H/I)IXXX(I/L) wherein X represents any amino acid, natural or not, such as copeptides chosen among fragments of co-activators of transcription, especially those of the p160 family, and more particularly among fragments of the co-activators SRC1, such as the fragment 686-700 of SRC1, or among fragments of co-repressors of 25 transcription.
  - 9. Nucleotide sequence coding for a polypeptide according to any one of claims 1 to 7.
- . 30 10. Nucleotide sequence according to claim 9, associated to elements necessary for the transcription of this sequence, particularly a promoter and a terminator of transcription.
- 11. Vector, particularly plasmid, comprising a nucleotide sequence according to 35 claim 9 or 11.
  - 12. Host cells, such as E.coli, transformed with a vector according to claim 11.
  - 13. Process for obtaining a polypeptide according to any one of claims 1 to 7, or a molecular complex according to claim 10, characterized in that it comprises:

- a step of transforming host cells with a nucleotide sequence according to claim 9 or

10, using a vector according to claim 11,

- a step of cultivating the transformed host cell according to claim 12 thus obtained, in an appropriate culture medium,

45 - and the recovery, and if necessary, the purification of the recombinant polypeptide or molecular complex obtained.

14. A crystal comprising a polypeptide according to any one of claims 1 to 9, or a molecular complex according to claim 10.

15. A crystal according to claim 14, characterized in that said crystal diffracts to at least 3 angstrom resolution and has a crystal stability within 5% of its unit cell dimensions.

55 16. A crystal according to claim 14 or 15, wherein the ROR-LBD has the following unit cell dimensions in angstroms: a= 52.302 Å, b= 58.490 Å and c= 106.036 Å,  $\alpha=\beta=\chi=90$ °, and an orthorhombic space group P212121.

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- 17. A crystal according to any one of claims 14 to 16, such as obtained by carrying out a process according to claim 13, and comprising a step of crystallisation in aqueous solvents of the polypeptides any one of claims 1 to 7, or the molecular complexes according to claim 8, especially at 4°C by the hanging drop vapour diffusion method,
- 18. Use of the polypeptides according to any one of claims 1 to 7, or of the molecular complexes according to claim 10, or of the crystals according to any one of claims 14 to 17, for carrying out:
- a process for the screening of a ROR-LBD ligand which is an agonist, or an antagonist of said receptor, or for the screening of ligands that perturb the structure of the receptor and having an effect on the recruitment of cofactors (co-activators and co-repressors) and hence on gene regulation,

- or a process for the analysis of the tridimensional structure of the complexes formed with said polypeptides, molecular complexes or crystals and a particular compound.

19. Use according to claim 18, for the screening of compounds acting as agonists or antagonists of ROR, said compounds being useful in the frame of the treatment of pathologies related to the central nervous system, the retinal organisation, the sensorial signal integration, the motricity, and sterility.

20. Process for the screening of a ROR-LBD ligand which is an agonist, or an antagonist of said receptor, said process comprising the following steps:

- contacting a polypeptide according to any one of claims 1 to 7, or a molecular complex according to claim 8, or a crystal according to any one of claims 14 to 17, advantageously linked to a solid support, with the particular compound susceptible to be a ROR-LBD ligand, preferably one of the said polypeptide, or molecular complex, or crystal, or tested ligand, being labelled, such as with a fluorescent, radioactive or enzymatic label,
- 30 detection of the possible association between the said polypeptide, or molecular complex, or crystal, and the tested ligand, by measuring the used label, especially after rinsing the support used in the preceding step, or by mass spectrometry under non denaturing conditions.
- 21. Process for the analysis of the tridimensional structure of the complexes formed with a polypeptide according to any one of claims 1 to 7, or a molecular complex according to claim 8, or a crystal according to any one of claims 14 to 17, and a particular compound susceptible to be a ROR-LBD ligand, said process comprising the following steps:

   contacting the said polymentide or molecular according to the said polymentide or molecular according to the said polymentide.
  - contacting the said polypeptide, or molecular complex, or crystal, with said particular compound.
  - crystallisation of the complex formed between the said polypeptide, or molecular complex, or crystal, and the tested ligand, especially with the vapour diffusion method, and tridimensional analysis of said complex, especially with the molecular replacement method,
  - or tridimensional analysis of said complex in soluble state, by using an appropriate method such as NMR.

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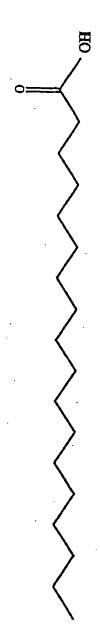


figure 1

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		_		L	E		С													_	-
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	Q	С	A	I	Q	I	T	.H	A	I	Q	Y	v	V	E	F	A	K	R	I	_
	AC	AGG	CTT	CAT	'GGA	GCT	GTG	TCA	.GAA	CGA	TCA	GAT	CTT	'AC'	TC	rga <i>i</i>	GT	CAG	3ጥጥ(	GCTTG	
241							+				+									GAAC	300
																			CAAC	CGAAC	
	T	G	F	М.	E	L	С	Q		, D						K			_	L	-
301	GA	AGT	3GT	TTT	AGT	GAG	AAT	GTG	CCG	TGC	CTI	'CAA	CCC	TTA	'AAA'	CAA	CAC	CTG	rtci	GTTT	
	CT.	CAC	CCA	AAA	TCA	CTC	TTA	CAC	GGC	ACG	+ GAA	 GTT	'GGG	TAA	TTT	. – – - СТТ	GTO	 3001		CAAA	360
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	GAZ	AGGI	AA	ATA	TGG.	AGG	AAT	GCA.	ААТ	GTT	CAA	ልርር	ירידיםי	'A CC	ሙጥር	יידירי א	TO 7		n »		
361				-+-			+				+										420
	CII			LAI.	ACC	rcc	TTA	CGT	TTA	CAA	GTT	TCG	GAA	TCC	AAG	ACT	'AC'I	rgg <i>p</i>	ATCA	CTTA	
	E						M														-
177	GAA	AGCA	TT?	rga(	CTT'	TGC	GAA	GAA'	TCT(	GTG'	TTC	CTT	GCA	GCT	GA <sup>†</sup> C	CGA	.GGA	AGA	GAT	TGCT	
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	E						ĸ								CIG	GCI	CCI	ICI	CIA	ACGA	
										C					T	E	E	E	I	A	-
81	CTG	TTC	TCC	TC:	rgc:	rgt'	CTC	ŞĄT/	ATC	CCC	AGA	CCG.	AGC	CTG	GĊT	GTT	AGA	ACC	'AAG	AAAA +	
	GAC	AAG	AGG	AG	ACG2	ACA	AGA	TAT	rago	GG?	CT	GGC'	TCG	GAC	CGA	CAA	+ TCT	TGG	TTC	TTTT	540
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## FIGURE 2

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541	GT	GTCCAGAAGCTTCAGGAAAAATTTATTTTGCACTTCAACATGTGATTCAGAAGAATCAC																			
	CAGGTCTTCGAAGTCCTTTTTTAAATAAAACGTGAAGTTGTACACTAAGTCTTCTTAGTG  V Q K L Q E K I Y F A L Q H V I Q K N H  CTGGATGATGAGACCCTGGCAAAGTTAATAGCCAAGATACCAACTATCACGGCAGTCTGC  GACCTACTACTCTGGGACCGTTTCAATTATCGGTTCTATGGTTGATAGTGCCGTCAGACG  L D D E T L A K L I A K I P T I T A V C  AACTTGCATGGGGAGAAGCTACAGGTATTTAAGCAGTCTCATCCAGACATAGTGAATACA  TTGAACGTACCCCTCTTCGATGTCCATAAATTCGTCAGAGTAGTGTATCACTTATGT  N L H G E K L Q V F K Q S H P D I V N T  CTGTTTCCTCCATTGTACAAGGAGCTCTTTTAATCCTGACTGTGCTGCGGTCTGCAAATGA			600																	
	V	Q	K	L	Q	E	K	1	Y	F	A	L	Q	H	V	I	Q	ĸ	N	H	-
501				-+-			+				+			-+-							660
	GA	CCT	ACT	ACT	CTG	GGA	.CCG	TTT	CAA	TTA	TCG	GTT	CTA	TGG	TTG	ATA	GTG	CCG	TCA	GACG	000
	L	D	D	E	T	L	A	K	L	I	A	К	I	P	T	I	T	A	v	C	-
61	AA	CTT 	GCA	TGG	GGA	GAA	GCT	ACA	GGT	ATT	TAA	GCA	GTC	TCA	TCC	AGA	CAT	AGT	GAA	TACA	
	TT	GAA	CGT.	ACC	CCT	CTT	CGA	TGT	CCA	TAA	ATT	CGT	CAG	AGT	AGG	TCT	GTA	TCA	CTT	ATGT	720
	N	L	H	G	E	ĸ	L	Q	V	<b>F</b> .	K	Q	s	н	P	ם	1	v	N	T	-
21	CT	GTT 	TCC'	TCC.	ATT	GTA	CAA	GGA	GCT	CTT	TAA	TCC	TGA	CTG	TGC	TGC	GGT	CTG	CAA	ATGA	
		CAA	AGG.	AGG	TAA	CAT	GTT	CCT	CGA	GAA	ATT	AGG.	ACT	GAC	ACG.	ACG	CCA	GAC	 GTT	TACT	780
	L	F	P	P	L	Y	ĸ	E	L	F	N	P	D	C	A	А	V	C	ĸ	* .	_

FIGURE 2 (suite 1)

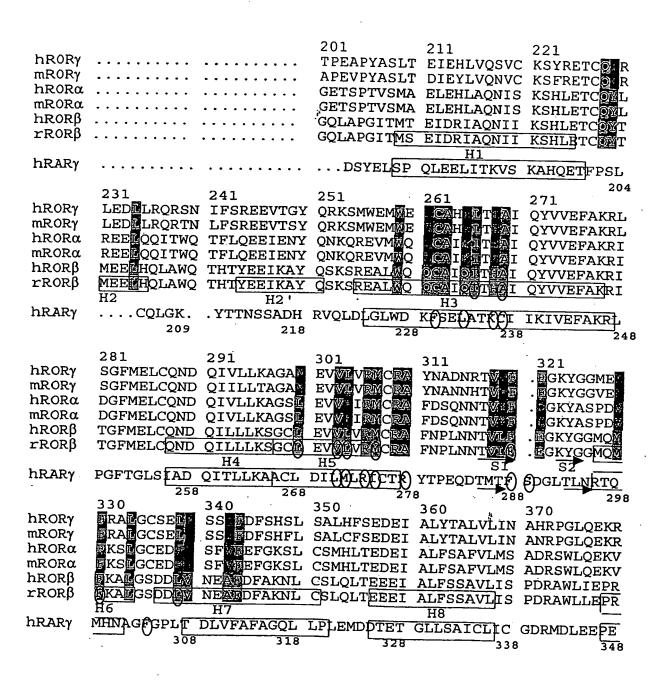


Figure 3

	380	390	400	409	419
hRORy	KVEQLQYNLE	LAFHHHLCKT	HR.QS.ILAK	LPPK.GKLRS	
mRORγ	RVEHLQYNLE	LAFHHHLCKT		LPPK.GKLRS	
hRORα	KIEKLQQKIQ	LALQHVLQKN		LICKVSTLRA	
mR0R $\alpha$	KIEKLQQKIQ	LALQHVLQKN	HREDG.ILTK	LICKVSTLRA	CGRETEKLM
hrorß	KVQKLQEKIY	FALQHVIQKN		<u>LIAKIPTITA</u>	MCNLEGEKLO
rRORβ	KVQKLQEKIY	FALQHVIQKN	HLDDE. TLAK	LIAKIPTITA	<b>WENLEGEKLQ</b>
	H9		H10	a H10	b H11
hRARγ	KVDKLQEPLL	EALRLYARRR	RPSQPYMFPR	MLMKITDLRG	ISTKGAERAI
	358	368	378	38	8 398
	429	439	449	459	
hR0Rγ	IFQHLHPIVV	QAAFPPLYKE	LFSTETESPV	GCPSDLEEGL	LASPYGLLAT
mRORγ	IFQHLHPIVV	QAAFPPLMKE	LFSTDVESPE	GLSK	
hRORα	AFKAIYPDIV	RLHFPPLYKE	LFTSEFEPAM	QIDG	
mRORα	AFKAIYPDIV	RLHFPPL <b>Y</b> KE	LFTSEFEPAM	QIDG	
hRoRβ	VFKQSHPEIV	NTLFPPLOKE	LFNPDCATAC	K	
rRORβ	VFKQSHPDIV	NTLFPPLXKE	LFNPDCAAVC	K	
	н11	H12	<del></del>		
hRARγ	TEKMELPG	PMPPLIRE	MLENPEMFED	DSSQPGPHPN	ASSEDEVPGG
	406	414	J 424	43	4 444

Figure 3 (suite 1)

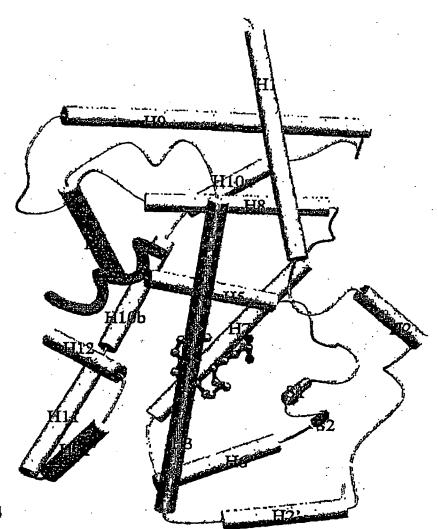


Figure 4

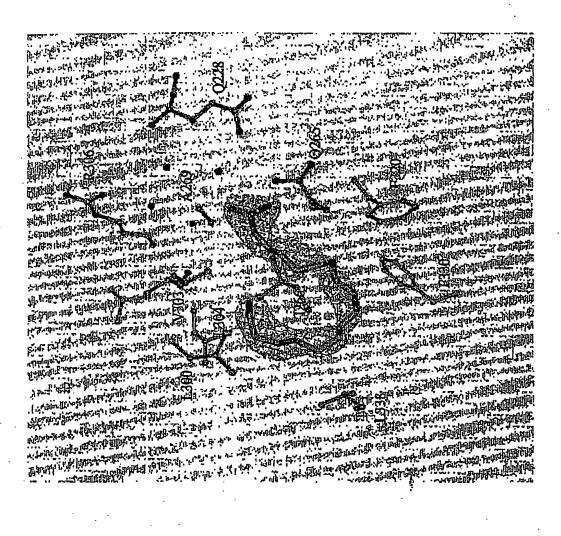


Figure 5

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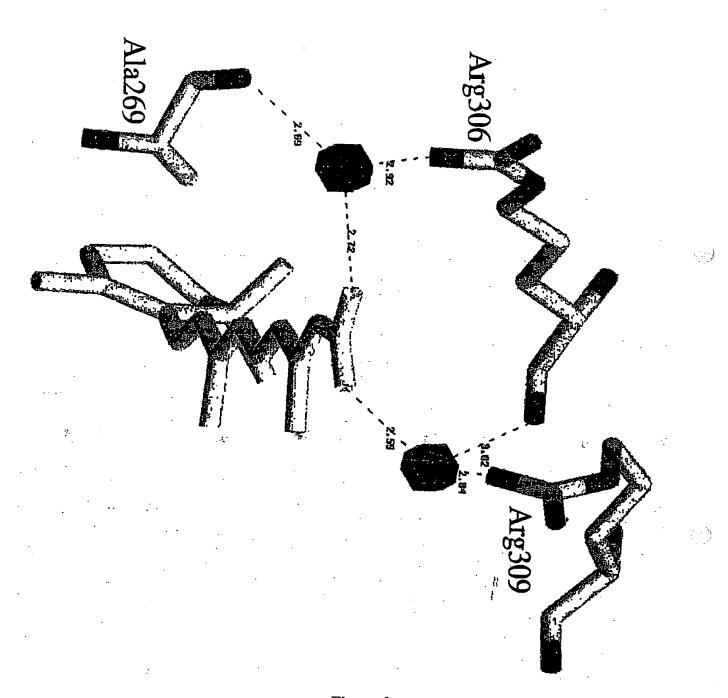
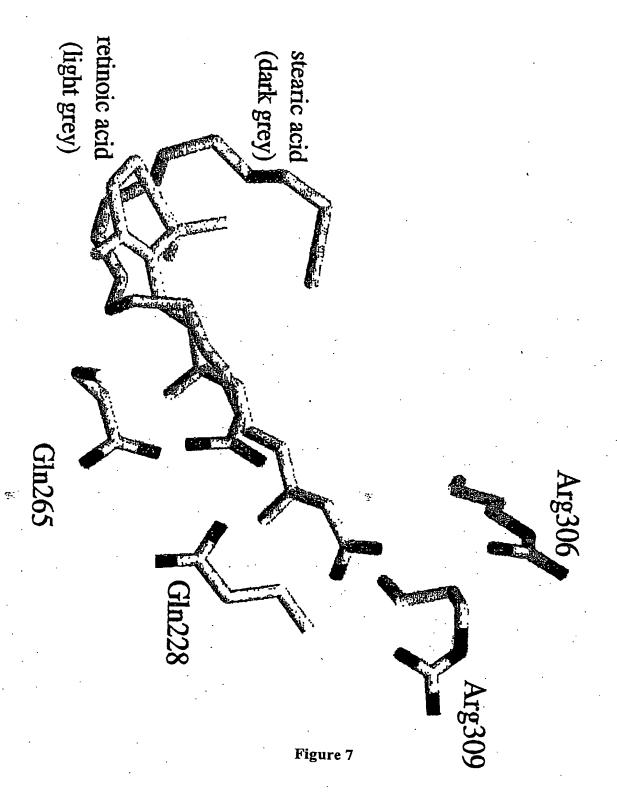
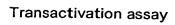
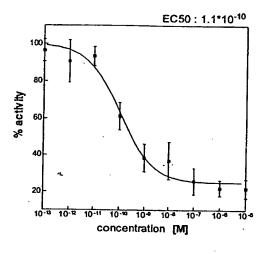


Figure 6



 $l^{\pm}:$ 





# Binding assay

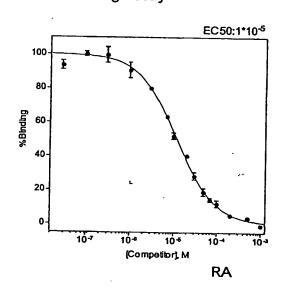


Figure 8

### SEQUENCE LISTING

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<120								RET]				ELATE	ED OF	RPHAN	1	
<130	> IC	)B 01	CNF	ROF	RB											
<1402 <1412																
<160	> 37	7														
<170	> Pa	tent	:In V	/er.	2.1											
<210; <211; <212; <213;	> 73 > DN	ΙA	.cial	. Sec	Jueno	e										
<220 <223	> De		-					Sequ gment					è			
<220 <221 <222	> CE		(732)													
<4002 atg t Met S	tct															48
gag a Glu 1																96
acc o					_		_	_			_	-				144
gct o																192
gtg ( Val V 65																240
aac ( Asn <i>l</i>																288
gtg a Val 1																336
gaa ( Glu (																384

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gad	cta Lei 130	u va.	g aat l Ası	t gaa n Gli	a gca u Ala	ttta Phe	e Asp	ttt Phe	gco Ala	g aa a Ly	g aa s Asi 14	n Le	g tg u Cy	t tc	c ttg r Leu
cag Gln 145	і теі	g aco	c gaç r Glı	g gaa ı Glı	a gaq ı Glı 150	ı Ile	get Ala	ctç Lev	g tto Phe	c to e Se: 15:	r Se	t ge	t gt a Va.	t cto 1 Le	g ata u Ile 160
tcc Ser	Pro	a gad o Asp	c cga Arg	g gco g Ala 165	ı Trp	ctg Leu	tta Lev	gaa Glu	Pro	Arq	a aaa g Lys	a gto s Val	caq l Gli	g aaq n Lys 175	g ctt s Leu 5
cạg Gln	gaa Glu	a aaa 1 Lys	att Ile 180	ryr	ttt Phe	gca Ala	ctt Leu	caą Gln 185	His	gto Val	g att L Ile	caç Glr	g aaq n Lys 190	s 'Asr	cac His
ctg Leu	gat Asp	gat Asp 195	) Glu	acc Thr	ctg Leu	gca Ala	aag Lys 200	Leu	ata Ile	gco Ala	aag Lys	1 ata 11e 205	Pro	act Thr	atc Ile
acg Thr	gca Ala 210	vai	tgc Cys	aac Asn	ttg Leu	cat His 215	Gly	gag Glu	aag Lys	cta Leu	cag Gln 220	Val	ttt Phe	aag Lys	cag Gln
tct Ser 225	cat His	cca Pro	gac Asp	ata Ile	gtg Val 230	Asn	aca Thr	ctg Leu	ttt Phe	cct Pro 235	Pro	ttg Leu	tac Tyr	aag Lys	gág Glu 240
			cct Pro											٠	
<211 <212 <213	3> D	RT rtif escr	icia iptio nce o	on o	f Art	tific	cial fraç	Se <b>ģ</b> ī gment	uence c of	e: n rat	ucle ROR	otid B	e		
1et	)> 2 Ser	Glu	Ile	Asp	Arg	Ile	Ala	Gln	Asn	Ile	Ile	Lys	Ser	His	Leu
1				5					10					,15	
ilu	Thr	Cys	Gln 20	Tyr	Thr	Met	Glu	Glu 25	Leu	His	Gln	Leu	Ala 30	Trp	Gln
hr	His	Thr 35	Tyr	Glu	Glu	Ile	Lys 40	Ala	Tyr	Gln	Ser	Lys 45	Ser	Arg	Glu
la	Leu 50	Trp	Gln	Gln	Cys	Ala 55	Ile	Gln	Ile	Thr	His 60	Ala	Ile	Gln	Tyr
'al 65	Val	Glu	Phe	Ala	Lys .70	Arg	Ile	Thr	Gly	Phe 75	Met	Ğlu	Leu	Cys	Gln 80
sn .	Asp	Gln	Ile	Leu 85	Leu	Leu	Lys	Ser	Gly 90	Cys	Leu	Glu	Val	Val 95	Leu
al .	Arg	Met	Cys 100	Arg	Ala	Phe	Asn	Pro 105	Leu	Asn	Asn	Thr	Val 110	Leu	Phe

Glu Gly Lys Tyr Gly Gly Met Gln Met Phe Lys Ala Leu Gly Ser Asp 115 120 125

- Asp Leu Val Asn Glu Ala Phe Asp Phe Ala Lys Asn Leu Cys Ser Leu 130 135 140
- Gln Leu Thr Glu Glu Glu Ile Ala Leu Phe Ser Ser Ala Val Leu Ile 145 150 155 160
- Ser Pro Asp Arg Ala Trp Leu Leu Glu Pro Arg Lys Val Gln Lys Leu 165 170 175
- Gln Glu Lys Ile Tyr Phe Ala Leu Gln His Val Ile Gln Lys Asn His 180 185 190
- Leu Asp Asp Glu Thr Leu Ala Lys Leu Ile Ala Lys Ile Pro Thr Ile 195 200 205
- Thr Ala Val Cys Asn Leu His Gly Glu Lys Leu Gln Val Phe Lys Gln 210 215 220
- Ser His Pro Asp Ile Val Asn Thr Leu Phe Pro Pro Leu Tyr Lys Glu 225 230 235 240

Leu Phe Asn Pro

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<211> 244

<2:12> PRT

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<220>

- <223> Description of Artificial Sequence: fragment of human  $\mbox{ROR}\beta$
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- Thr His Thr Tyr Glu Glu Ile Lys Ala Tyr Gln Ser Lys Ser Arg Glu 35 40 45
- Ala Leu Trp Gln Gln Cys Ala Ile Gln Ile Thr His Ala Ile Gln Tyr 50 55 60
- Val Val Glu Phe Ala Lys Arg Ile Thr Gly Phe Met Glu Leu Cys Gln 65 70 75 80
- Asn Asp Gln Ile Leu Leu Leu Lys Ser Gly Cys Leu Glu Val Val Leu 85 90 95
- Val Arg Met Cys Arg Ala Phe Asn Pro Leu Asn Asn Thr Val Leu Phe 100 105 110

Glu Gly Lys Tyr Gly Gly Met Gln Met Phe Lys Ala Leu Gly Ser Asp 115 120 125

Asp Leu Val Asn Glu Ala Phe Asp Phe Ala Lys Asn Leu Cys Ser Leu 130 135 140

Gln Leu Thr Glu Glu Glu Ile Ala Leu Phe Ser Ser Ala Val Leu Ile 145 150 155 160

Ser Pro Asp Arg Ala Trp Leu Ile Glu Pro Arg Lys Val Gln Lys Leu 165 170 175

Gln Glu Lys Ile Tyr Phe Ala Leu Gln His Val Ile Gln Lys Asn His 180 185 190

Leu Asp Asp Glu Thr Leu Ala Lys Leu Ile Ala Lys Ile Pro Thr Ile 195 200 205

Thr Ala Val Cys Asn Leu His Gly Glu Lys Leu Gln Val Phe Lys Gln 210 215 220

Ser His Pro Glu Ile Val Asn Thr Leu Phe Pro Pro Leu Tyr Lys Glu 225 230 235 240

Leu Phe Asn Pro

<210> 4

₫.

<211> 242

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: fragment of human ROR $\gamma$ 

<400> 4

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1 5 10 15

Glu Thr Cys Gln Leu Arg Leu Glu Asp Leu Leu Arg Gln Arg Ser Asn 20 25 30 .

Ile Phe Ser Arg Glu Glu Val Thr Gly Tyr Gln Arg Lys Ser Met Trp 35 40 45

Glu Met Trp Glu Arg Cys Ala His His Leu Thr Glu Ala Ile Gln Tyr
50 55 60

Val Val Glu Phe Ala Lys Arg Leu Ser Gly Phe Met Glu Leu Cys Gln
65 70 75 80

Asn Asp Gln Ile Val Leu Leu Lys Ala Gly Ala Met Glu Val Val Leu
85 90 05

Val Arg Met Cys Arg Ala Tyr Asn Ala Asp Asn Arg Thr Val Phe Phe 100 105 110

Glu Gly Lys Tyr Gly Gly Met Glu Leu Phe Arg Ala Leu Gly Cys Ser 115 120 125 Glu Leu Ile Ser Ser Ile Phe Asp Phe Ser His Ser Leu Ser Ala Leu 130 135 140

His Phe Ser Glu Asp Glu Ile Ala Leu Tyr Thr Ala Leu Val Leu Ile 145 150 155 160

Asn Ala His Arg Pro Gly Leu Gln Glu Lys Arg Lys Val Glu Gln Leu 165 170 175

Gln Tyr Asn Leu Glu Leu Ala Phe His His His Leu Cys Lys Thr His 180 185 190

Arg Gln Ser Ile Leu Ala Lys Leu Pro Pro Lys Gly Lys Leu Arg Ser 195 200 205 \_\_\_\_\_\_

Leu Cys Ser Gln His Val Glu Arg Leu Gln Ile Phe Gln His Leu His 210 215 220

Pro Ile Val Val Gln Ala Ala Phe Pro Pro Leu Tyr Lys Glu Leu Phe 225 230 235 240

Ser Thr

<210> 5

<211> 242

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: fragment of murine RORy

<400> 5

Leu Thr Asp Ile Glu Tyr Leu Val Gln Asn Val Cys Lys Ser Phe Arg
1 5 10 15

Glu Thr Cys Gln Leu Arg Leu Glu Asp Leu Leu Arg Gln Arg Thr Asn 20 25 30

Leu Phe Ser Arg Glu Glu Val Thr Ser Tyr Gln Arg Lys Ser Met Trp 35 40 45

Glu Met Trp Glu Arg Cys Ala His His Leu Thr Glu Ala Ile Gln Tyr 50 55 60

Val Val Glu Phe Ala Lys Arg Leu Ser Gly Phe Met Glu Leu Cys Gln 65 70 75 80

Asn Asp Gln Ile Ile Leu Leu Thr Ala Gly Ala Met Glu Val Val Leu 85 90 95

Val Arg Met Cys Arg Ala Tyr Asn Ala Asn Asn His Thr Val Phe 100 105 110

Glu Gly Lys Tyr Gly Gly Val Glu Leu Phe Arg Ala Leu Gly Cys Ser 115 120 125

Glu Leu Ile Ser Ser Ile Phe Asp Phe Ser His Phe Leu Ser Ala Leu 130 135 140

Cys Phe Ser Glu Asp Glu Ile Ala Leu Tyr Thr Ala Leu Val Leu Ile 145 150 155 160

Asn Ala Asn Arg Pro Gly Leu Gln Glu Lys Arg Arg Val Glu His Leu 165 170 175

Gln Tyr Asn Leu Glu Leu Ala Phe His His His Leu Cys Lys Thr His 180 185 190

Arg Gln Gly Leu Leu Ala Lys Leu Pro Pro Lys Gly Lys Leu Arg Ser 195 200 205

Leu Cys Ser Gln His Val Glu Lys Leu Gln Ile Phe Gln His Leu His 210 215 220

Pro Ile Val Val Gln Ala Ala Phe Pro Pro Leu Tyr Lys Glu Leu Phe 225 235 240

Ser Thr

<210> 6

<211> 244

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: fragment of human  $ROR\alpha$ 

<400> 6

Met Ala Glu Leu Glu His Leu Ala Gln Asn Ile Ser Lys Ser His Leu 1 5 10 15

Glu Thr Cys Gln Tyr Leu Arg Glu Glu Leu Gln Gln Ile Thr Trp Gln 20 25 30

Thr Phe Leu Gln Glu Glu Ile Glu Asn Tyr Gln Asn Lys Gln Arg Glu 35 40 45

Val Met Trp Gln Leu Cys Ala Ile Lys Ile Thr Glu Ala Ile Gln Tyr 50 55 60

Val Val Glu Phe Ala Lys Arg Ile Asp Gly Phe Met Glu Leu Cys Gln 65 70 75 80

Asn Asp Gln Ile Val Leu Leu Lys Ala Gly Ser Leu Glu Val Val Phe
85 90 95

Ile Arg Met Cys Arg Ala Phe Asp Ser Gln Asn Asn Thr Val Tyr Phe
100 105 110

Asp Gly Lys Tyr Ala Ser Pro Asp Val Phe Lys Ser Leu Gly Cys Glu 115 120 125

Asp Phe Ile Ser Phe Val Phe Glu Phe Gly Lys Ser Leu Cys Ser Met 130 135 140

His Leu Thr Glu Asp Glu Ile Ala Leu Phe Ser Ala Phe Val Leu Met 145 150 155 160

Ser Ala Asp Arg Ser Trp Leu Gln Glu Lys Val Lys Ile Glu Lys Leu 165 170 175

Gln Gln Lys Ile Gln Leu Ala Leu Gln His Val Leu Gln Lys Asn His 180 185 190

Arg Glu Asp Gly Ile Leu Thr Lys Leu Ile Cys Lys Val Ser Thr Leu 195 200 205

Arg Ala Leu Cys Gly Arg His Thr Glu Lys Leu Met Ala Phe Lys Ala 210 215 220

Ile Tyr Pro Asp Ile Val Arg Leu His Phe Pro Pro Leu Tyr Lys Glu 225 230 235 240

Leu Phe Thr Ser

<210> 7

<211> 244

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: fragment of murine  $\mbox{ROR}\alpha$ 

<400> 13

Met Ala Glu Leu Glu His Leu Ala Gln Asn Ile Ser Lys Ser His Leu 1 5 10 15

Glu Thr Cys Gln Tyr Leu Arg Glu Glu Leu Gln Gln Ile Thr Trp Gln 20 25 30

Thr Phe Leu Gln Glu Glu Ile Glu Asn Tyr Gln Asn Lys Gln Arg Glu
35 40 45

Val Met Trp Gln Leu Cys Ala Ile Lys Ile Thr Glu Ala Ile Gln Tyr 50 55 60

Val Val Glu Phe Ala Lys Arg Ile Asp Gly Phe Met Glu Leu Cys Gln 65 70 75 80

Asn Asp Gln Ile Val Leu Lys Ala Gly Ser Leu Glu Val Val Phe 85 90 95

Ile Arg Met Cys Arg Ala Phe Asp Ser Gln Asn Asn Thr Val Tyr Phe 100 105 110

Asp Gly Lys Tyr Ala Ser Pro Asp Val Phe Lys Ser Leu Gly Cys Glu 115 120 125

Asp Phe Ile Ser Phe Val Phe Glu Phe Gly Lys Ser Leu Cys Ser Met 130 135 140

His Leu Thr Glu Asp Glu Ile Ala Leu Phe Ser Ala Phe Val Leu Met 145 150 155 160

- Ser Ala Asp Arg Ser Trp Leu Gln Glu Lys Val Lys Ile Glu Lys Leu 165 170 175
- Gln Gln Lys Ile Gln Leu Ala Leu Gln His Val Leu Gln Lys Asn His 180 185 190
- Arg Glu Asp Gly Ile Leu Thr Lys Leu Ile Cys Lys Val Ser Thr Leu 195 200 205
- Arg Ala Leu Cys Gly Arg His Thr Glu Lys Leu Met Ala Phe Lys Ala 210 215 220
- Ile Tyr Pro Asp Ile Val Arg Leu His Phe Pro Pro Leu Tyr Lys Glu 225 235 240

Leu Phe Thr Ser

<210> 8

<211> 245

<212> PRT

- <213> Artificial Sequence
- <223> Description of Artificial Sequence: nucleotide sequence coding for a fragment of rat ROR $\beta$

<400> 8

- Thr Met Ser Glu Ile Asp Arg Ile Ala Gln Asn Ile Ile Lys Ser His 1 5 10 15
- Leu Glu Thr Cys Gln Tyr Thr Met Glu Glu Leu His Gln Leu Ala Trp 20 25 30
- Gln Thr His Thr Tyr Glu Glu Ile Lys Ala Tyr Gln Ser Lys Ser Arg
  35 40 45
- Glu Ala Leu Trp Gln Gln Cys Ala Ile Gln Ile Thr His Ala Ile Gln 50 60
- Tyr Val Val Glu Phe Ala Lys Arg Ile Thr Gly Phe Met Glu Leu Cys 65 70 75 80
- Gln Asn Asp Gln Ile Leu Leu Leu Lys Ser Gly Cys Leu Glu Val Val 85 90 95
- Leu Val Arg Met Cys Arg Ala Phe Asn Pro Leu Asn Asn Thr Val Leu 100 105 110
- Phe Glu Gly Lys Tyr Gly Gly Met Gln Met Phe Lys Ala Leu Gly Ser 115 120 125
- Asp Asp Leu Val Asn Glu Ala Phe Asp Phe Ala Lys Asn Leu Cys Ser 130 135 140
- Leu Gln Leu Thr Glu Glu Glu Ile Ala Leu Phe Ser Ser Ala Val Leu 145 150 155 160

Ile Ser Pro Asp Arg Ala Trp Leu Leu Glu Pro Arg Lys Val Gln Lys 165 170 175

Leu Gln Glu Lys Ile Tyr Phe Ala Leu Gln His Val Ile Gln Lys Asn 180 185 190

His Leu Asp Asp Glu Thr Leu Ala Lys Leu Ile Ala Lys Ile Pro Thr 195 200 205

Ile Thr Ala Val Cys Asn Leu His Gly Glu Lys Leu Gln Val Phe Lys 210 220

Gln Ser His Pro Asp Ile Val Asn Thr Leu Phe Pro Pro Leu Tyr Lys 225 230 235 240

Glu Leu Phe Asn Pro

<210> 9

<211> 245

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: fragment of human ROR $\beta$ 

<400> 9

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Thr Met Thr Glu Ile Asp Arg Ile Ala Gln Asn Ile Ile Lys Ser His 1 5 10 15

Leu Glu Thr Cys Gln Tyr Thr Met Glu Glu Leu His Gln Leu Ala Trp
20 25 30

Gln Thr His Thr Tyr Glu Glu Ile Lys Ala Tyr Gln Ser Lys Ser Arg 35 40 45

Glu Ala Leu Trp Gln Gln Cys Ala Ile Gln Ile Thr His Ala Ile Gln 50 60

Tyr Val Val Glu Phe Ala Lys Arg Ile Thr Gly Phe Met Glu Leu Cys 65 70 75 80

Gln Asn Asp Gln Ile Leu Leu Leu Lys Ser Gly Cys Leu Glu Val Val 85 90 95

Leu Val Arg Met Cys Arg Ala Phe Asn Pro Leu Asn Asn Thr Val Leu 100 105 110

Phe Glu Gly Lys Tyr Gly Gly Met Gln Met Phe Lys Ala Leu Gly Ser 115 120 125

Asp Asp Leu Val Asn Glu Ala Phe Asp Phe Ala Lys Asn Leu Cys Ser 130 135 140

Leu Gln Leu Thr Glu Glu Glu Ile Ala Leu Phe Ser Ser Ala Val Leu 145 150 155 160

Ile Ser Pro Asp Arg Ala Trp Leu Ile Glu Pro Arg Lys Val Gln Lys
165 170 175

Leu Gln Glu Lys Ile Tyr Phe Ala Leu Gln His Val Ile Gln Lys Asn 180 185 190

His Leu Asp Asp Glu Thr Leu Ala Lys Leu Ile Ala Lys Ile Pro Thr 195 200 205

Ile Thr Ala Val Cys Asn Leu His Gly Glu Lys Leu Gln Val Phe Lys 210 220

Gln Ser His Pro Glu Ile Val Asn Thr Leu Phe Pro Pro Leu Tyr Lys 225 230 235 240

Glu Leu Phe Asn Pro

<210> 10

<211> 243

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: fragment of human RORy

<400> 10

Ser Leu Thr Glu Ile Glu His Leu Val Gln Ser Val Cys Lys Ser Tyr
1 5 10 15

Arg Glu Thr Cys Gln Leu Arg Leu Glu Asp Leu Leu Arg Gln Arg Ser 20 25 30

Asn Ile Phe Ser Arg Glu Glu Val Thr Gly Tyr Gln Arg Lys Ser Met 35 40 45

Trp Glu Met Trp Glu Arg Cys Ala His His Leu Thr Glu Ala Ile Gln 50 55 60

Tyr Val Val Glu Phe Ala Lys Arg Leu Ser Gly Phe Met Glu Leu Cys 65 70 75 80

Gln Asn Asp Gln Ile Val Leu Leu Lys Ala Gly Ala Met Glu Val Val 85 90 '95

Leu Val Arg Met Cys Arg Ala Tyr Asn Ala Asp Asn Arg Thr Val Phe
100 105 110

Phe Glu Gly Lys Tyr Gly Gly Met Glu Leu Phe Arg Ala Leu Gly Cys 115 120 125

Ser Glu Leu Ile Ser Ser Ile Phe Asp Phe Ser His Ser Leu Ser Ala 130 135 140

Leu His Phe Ser Glu Asp Glu Ile Ala Leu Tyr Thr Ala Leu Val Leu 145 150 155 160

Ile Asn Ala His Arg Pro Gly Leu Gln Glu Lys Arg Lys Val Glu Gln 165 170 175

Leu Gln Tyr Asn Leu Glu Leu Ala Phe His His His Leu Cys Lys Thr 180 185 190

His Arg Gln Ser Ile Leu Ala Lys Leu Pro Pro Lys Gly Lys Leu Arg 195 200 205

Ser Leu Cys Ser Gln His Val Glu Arg Leu Gln Ile Phe Gln His Leu 210 215 220

His Pro Ile Val Val Gln Ala Ala Phe Pro Pro Leu Tyr Lys Glu Leu 225 230 235 240

Phe Ser Thr

<210> 11

<211> 243

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: fragment of murine RORy

<400> 11

Ser Leu Thr Asp Ile Glu Tyr Leu Val Gln Asn Val Cys Lys Ser Phe 1 5 10 15

Arg Glu Thr Cys Gln Leu Arg Leu Glu Asp Leu Leu Arg Gln Arg Thr 20 25 30

Asn Leu Phe Ser Arg Glu Glu Val Thr Ser Tyr Gln Arg Lys Ser Met 35 40 45

Trp Glu Met Trp Glu Arg Cys Ala His His Leu Thr Glu Ala Ile Gln 50 55 60

Tyr Val Val Glu Phe Ala Lys Arg Leu Ser Gly Phe Met Glu Leu Cys 65 70 75 80

Gln Asn Asp Gln Ile Ile Leu Leu Thr Ala Gly Ala Met Glu Val Val 85 90 ,95

Leu Val Arg Met Cys Arg Ala Tyr Asn Ala Asn Asn His Thr Val Phe 100 105 110

Phe Glu Gly Lys Tyr Gly Gly Val Glu Leu Phe Arg Ala Leu Gly Cys 115 120 125

Ser Glu Leu Ile Ser Ser Ile Phe Asp Phe Ser His Phe Leu Ser Ala 130 135 140

Leu Cys Phe Ser Glu Asp Glu Ile Ala Leu Tyr Thr Ala Leu Val Leu 145 150 155 160

Ile Asn Ala Asn Arg Pro Gly Leu Gln Glu Lys Arg Arg Val Glu His
165 170 175

Leu Gl<br/>n Týr Asn Leu Glu Leu Ala Phe His His His Leu Cys Lys Th<br/>r 180 185 190

 $\cdot$   $\cdot$   $\cdot$ 

His Arg Gln Gly Leu Leu Ala Lys Leu Pro Pro Lys Gly Lys Leu Arg 195 200 205

Ser Leu Cys Ser Gln His Val Glu Lys Leu Gln Ile Phe Gln His Leu 210 215 220

His Pro Ile Val Val Gln Ala Ala Phe Pro Pro Leu Tyr Lys Glu Leu 225 235 240

Phe Ser Thr

<210> 12

<211> 245

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: fragment of human ROR $\alpha$ 

<400> 12

Ser Met Ala Glu Leu Glu His Leu Ala Gln Asn Ile Ser Lys Ser His 1 5 10 15

Leu Glu Thr Cys Gln Tyr Leu Arg Glu Glu Leu Gln Gln Ile Thr Trp
20 25 30

Gln Thr Phe Leu Gln Glu Glu Ile Glu Asn Tyr Gln Asn Lys Gln Arg 35 40 45

Glu Val Met Trp Gln Leu Cys Ala Ile Lys Ile Thr Glu Ala Ile Gln 50 55 60

Tyr Val Val Glu Phe Ala Lys Arg Ile Asp Gly Phe Met Glu Leu Cys
65 70 75 80

Gln Asn Asp Gln Ile Val Leu Leu Lys Ala Gly Ser Leu Glu Val Val 85 90 95

Phe Ile Arg Met Cys Arg Ala Phe Asp Ser Gln Asn Asn Thr Val Tyr 100 105 110 !

Phe Asp Gly Lys Tyr Ala Ser Pro Asp Val Phe Lys Ser Leu Gly Cys
115 120 125

Glu Asp Phe Ile Ser Phe Val Phe Glu Phe Gly Lys Ser Leu Cys Ser 130 135 140

Met His Leu Thr Glu Asp Glu Ile Ala Leu Phe Ser Ala Phe Val Leu 145 150 155 160

Met Ser Ala Asp Arg Ser Trp Leu Gln Glu Lys Val Lys Ile Glu Lys 165 170 175

Leu Gln Gln Lys Ile Gln Leu Ala Leu Gln His Val Leu Gln Lys Asn 180 185 190

His Arg Glu Asp Gly Ile Leu Thr Lys Leu Ile Cys Lys Val Ser Thr 195 200 205

Leu Arg Ala Leu Cys Gly Arg His Thr Glu Lys Leu Met Ala Phe Lys 210 . 220

Ala Ile Tyr Pro Asp Ile Val Arg Leu His Phe Pro Pro Leu Tyr Lys 225 230 235 240

Glu Leu Phe Thr Ser

<210> 13

<211> 245

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: fragment of murine  $ROR\alpha$ 

<400> 13

Ser Met Ala Glu Leu Glu His Leu Ala Gln Asn Ile Ser Lys Ser His 1 5 10 15

Leu Glu Thr Cys Gln Tyr Leu Arg Glu Glu Leu Gln Gln Ile Thr Trp 20 25 30

Gln Thr Phe Leu Gln Glu Glu Ile Glu Asn Tyr Gln Asn Lys Gln Arg 35 40 45

Glu Val Met Trp Gln Leu Cys Ala Ile Lys Ile Thr Glu Ala Ile Gln
50 55 60

Tyr Val Val Glu Phe Ala Lys Arg Ile Asp Gly Phe Met Glu Leu Cys 65 70 75 80

Gln Asn Asp Gln Ile Val Leu Leu Lys Ala Gly Ser Leu Glu Val Val 85 90 95

Phe Ile Arg Met Cys Arg Ala Phe Asp Ser Gln Asn Asn Thr Val Tyr 100 105 110 ,

Phe Asp Gly Lys Tyr Ala Ser Pro Asp Val Phe Lys Ser Leu Gly Cys 115 120 125

Glu Asp Phe Ile Ser Phe Val Phe Glu Phe Gly Lys Ser Leu Cys Ser 130 135 140

Met His Leu Thr Glu Asp Glu Ile Ala Leu Phe Ser Ala Phe Val Leu 145 150 155 160

Met Ser Ala Asp Arg Ser Trp Leu Gln Glu Lys Val Lys Ile Glu Lys 165 170 175

Leu Gln Gln Lys Ile Gln Leu Ala Leu Gln His Val Leu Gln Lys Asn 180 185 190

His Arg Glu Asp Gly Ile Leu Thr Lys Leu Ile Cys Lys Val Ser Thr 195 200 205

,

Leu Arg Ala Leu Cys Gly Arg His Thr Glu Lys Leu Met Ala Phe Lys 210 215 220

Ala Ile Tyr Pro Asp Ile Val Arg Leu His Phe Pro Pro Leu Tyr Lys 225 230 235 240

Glu Leu Phe Thr Ser 245

<210> 14

<211> 244

<212> PRT

<213> Artificial Sequence

<223> Description of Artificial Seguence: nucleotide sequence coding for a fragment of rat  $ROR\beta$ 

<400> 14

Thr Met Ser Glu Ile Asp Arg Ile Ala Gln Asn Ile Ile Lys Ser His 1 5 10 15

Leu Glu Thr Cys Gln Tyr Thr Met Glu Glu Leu His Gln Leu Ala Trp 20 25 30

Gln Thr His Thr Tyr Glu Glu Ile Lys Ala Tyr Gln Ser Lys Ser Arg
35 40 45

Glu Ala Leu Trp Gln Gln Cys Ala Ile Gln Ile Thr His Ala Ile Gln 50 55 60

Tyr Val Val Glu Phe Ala Lys Arg Ile Thr Gly Phe Met Glu Leu Cys 65 70 75 80

Gln Asn Asp Gln Ile Leu Leu Leu Lys Ser Gly Cys Leu Glu Val Val 85 90 95

Leu Val Arg Met Cys Arg Ala Phe Asn Pro Leu Asn Asn Thr Val Leu 100 105 110

Phe Glu Gly Lys Tyr Gly Gly Met Gln Met Phe Lys Ala Leu Gly Ser 115 120 125

Asp Asp Leu Val Asn Glu Ala Phe Asp Phe Ala Lys Asn Leu Cys Ser

Leu Gln Leu Thr Glu Glu Glu Ile Ala Leu Phe Ser Ser Ala Val Leu 145 150 155 160

Ile Ser Pro Asp Arg Ala Trp Leu Leu Glu Pro Arg Lys Val Gln Lys
165 170 175

Leu Gln Glu Lys Ile Tyr Phe Ala Leu Gln His Val Ile Gln Lys Asn 180 185 190

His Leu Asp Asp Glu Thr Leu Ala Lys Leu Ile Ala Lys Ile Pro Thr 195 200 205

Ile Thr Ala Val Cys Asn Leu His Gly Glu Lys Leu Gln Val Phe Lys 210 215 220

Gln Ser His Pro Asp Ile Val Asn Thr Leu Phe Pro Pro Leu Tyr Lys 225 230 235 240

Glu Leu Phe Asn

<210> 15

<211> 244

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: fragment of human ROR $\beta$ 

<400> 15

Thr Met Thr Glu Ile Asp Arg Ile Ala Gln Asn Ile Ile Lys Ser His 1 5 10 15

Leu Glu Thr Cys Gln Tyr Thr Met Glu Glu Leu His Gln Leu Ala Trp
20 25 30

Gln Thr His Thr Tyr Glu Glu Ile Lys Ala Tyr Gln Ser Lys Ser Arg
35 40 45

Glu Ala Leu Trp Gln Gln Cys Ala Ile Gln Ile Thr His Ala Ile Gln 50 55 . 60

Tyr Val Val Glu Phe Ala Lys Arg Ile Thr Gly Phe Met Glu Leu Cys
65 70 75 80

Gln Asn Asp Gln Ile Leu Leu Lys Ser Gly Cys Leu Glu Val Val 85 90 95

Leu Val Arg Met Cys Arg Ala Phe Asn Pro Leu Asn Asn Thr Val Leu 100 105 110

Phe Glu Gly Lys Tyr Gly Gly Met Gln Met Phe Lys Ala Leu Gly Ser 115 120 125

Asp Asp Leu Val Asn Glu Ala Phe Asp Phe Ala Lys Asn Leu Cys Ser 130 135 140

Leu Gln Leu Thr Glu Glu Glu Ile Ala Leu Phe Ser Ser Ala Val Leu 145 150 155 160

Ile Ser Pro Asp Arg Ala Trp Leu Ile Glu Pro Arg Lys Val Gln Lys
165 170 175

Leu Gln Glu Lys Ile Tyr Phe Ala Leu Gln His Val Ile Gln Lys Asn 180 185 190

His Leu Asp Asp Glu Thr Leu Ala Lys Leu Ile Ala Lys Ile Pro Thr 195 200 205

Ile Thr Ala Val Cys Asn Leu His Gly Glu Lys Leu Gln Val Phe Lys 210 215 220

Gln Ser His Pro Glu Ile Val Asn Thr Leu Phe Pro Pro Leu Tyr Lys 225 230 235 240

Glu Leu Phe Asn

<210> 16

<211> 242

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: fragment of human RORy

<400> 16

Ser Leu Thr Glu Ile Glu His Leu Val Gln Ser Val Cys Lys Ser Tyr
1 5 10 15

Arg Glu Thr Cys Gln Leu Arg Leu Glu Asp Leu Leu Arg Gln Arg Ser 20 25 30

Asn lle Phe Ser Arg Glu Glu Val Thr Gly Tyr Gln Arg Lys Ser Met
35 40 45

Trp Glu Met Trp Glu Arg Cys Ala His His Leu Thr Glu Ala Ile Gln 50 55 60

Tyr Val Val Glu Phe Ala Lys Arg Leu Ser Gly Phe Met Glu Leu Cys
65 70 75 80

Gln Asn Asp Gln Ile Val Leu Leu Lys Ala Gly Ala Met Glu Val Val 85 90 95

Leu Val Arg Met Cys Arg Ala Tyr Asn Ala Asp Asn Arg Thr Val Phe
100 105 110

Phe Glu Gly Lys Tyr Gly Gly Met Glu Leu Phe Arg Ala Leu Gly Cys 115 120 125

Ser Glu Leu Ile Ser Ser Ile Phe Asp Phe Ser His Ser Leu Ser Ala 130 135 140

Leu His Phe Ser Glu Asp Glu Ile Ala Leu Tyr/Thr Ala Leu Val Leu 145 150 155 160

Ile Asn Ala His Arg Pro Gly Leu Gln Glu Lys Arg Lys Val Glu Gln 165 170 175

Leu Gln Tyr Asn Leu Glu Leu Ala Phe His His His Leu Cys Lys Thr 180 185 190

His Arg Gln Ser Ile Leu Ala Lys Leu Pro Pro Lys Gly Lys Leu Arg

Ser Leu Cys Ser Gln His Val Glu Arg Leu Gln Ile Phe Gln His Leu 210 215 220

His Pro Ile Val Val Gln Ala Ala Phe Pro Pro Leu Tyr Lys Glu Leu 225 230 235 240

Phe Ser

<210> 17 <211> 242 <212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: fragment of murine RORy

<400> 17
Ser Leu Thr Asp Ile Glu Tyr Leu Val Gln Asn Val Cys Lys Ser Phe
1 5 10 15

Arg Glu Thr Cys Gln Leu Arg Leu Glu Asp Leu Leu Arg Gln Arg Thr 20 25 30

Asn Leu Phe Ser Arg Glu Glu Val Thr Ser Tyr Gln Arg Lys Ser Met 35 40 45

Trp Glu Met Trp Glu Arg Cys Ala Ḥis His Leu Thr Glu Ala Ile Gln 50 55 60

Tyr Val Val Glu Phe Ala Lys Arg Leu Ser Gly Phe Met Glu Leu Cys 65 70 75 80

Gln Asn Asp Gln Ile Ile Leu Leu Thr Ala Gly Ala Met Glu Val Val 85 90 95

Leu Val Arg Met Cys Arg Ala Tyr Asn Ala Asn Asn His Thr Val Phe 100 105 110

Phe Glu Gly Lys Tyr Gly Gly Val Glu Leu Phe Arg Ala Leu Gly Cys 115 120 125

Ser Glu Leu Ile Ser Ser Ile Phe Asp Phe Ser His Phe Leu Ser Ala 130 135 140

Leu Cys Phe Ser Glu Asp Glu Ile Ala Leu Tyr Thr Ala Leu Val Leu 145 150 155 160

Ile Asn Ala Asn Arg Pro Gly Leu Gln Glu Lys Arg Arg Val Glu His
165 170 175

Leu Gln Tyr Asn Leu Glu Leu Ala Phe His His His Leu Cys Lys Thr 180 185 190

His Arg Gln Gly Leu Leu Ala Lys Leu Pro Pro Lys Gly Lys Leu Arg 195 200 205

Ser Leu Cys Ser Gln His Val Glu Lys Leu Gln Ile Phe Gln His Leu 210 215 220

His Pro Ile Val Val Gln Ala Ala Phe Pro Pro Leu Tyr Lys Glu Leu 225 230 235 240

Phe Ser

<210> 18 <211> 244

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: fragment of human  $ROR\alpha$ 

<400> 18

Ser Met Ala Glu Leu Glu His Leu Ala Gln Asn Ile Ser Lys Ser His  $1 \hspace{1cm} 5 \hspace{1cm} 10 \hspace{1cm} 15$ 

Leu Glu Thr Cys Gln Tyr Leu Arg Glu Glu Leu Gln Gln Ile Thr Trp 20 25 30

Gln Thr Phe Leu Gln Glu Glu Ile Glu Asn Tyr Gln Asn Lys Gln Arg 35 40 45

Glu Val Met Trp Gln Leu Cys Ala Ile Lys Ile Thr Glu Ala Ile Gln 50 60

Tyr Val Val Glu Phe Ala Lys Arg Ile Asp Gly Phe Met Glu Leu Cys
65 70 75 80

Gln Asn Asp Gln Ile Val Leu Leu Lys Ala Gly Ser Leu Glu Val Val 85 90 95

Phe Ile Arg Met Cys Arg Ala Phe Asp Ser Gln Asn Asn Thr Val Tyr 100 105 110

Phe Asp Gly Lys Tyr Ala Ser Pro Asp Val Phe Lys Ser Leu Gly Cys 115 120 125

Glu Asp Phe Ile Ser Phe Val Phe Glu Phe Gly Lys Ser Leu Cys Ser 130 135 140

Met His Leu Thr Glu Asp Glu Ile Ala Leu Phe Ser Ala Phe Val Leu 145 150 155 160

Met Ser Ala Asp Arg Ser Trp Leu Gln Glu Lys Val Lys Ile Glu Lys 165 170 175

Leu Gln Gln Lys Ile Gln Leu Ala Leu Gln His Val Leu Gln Lys Asn 180 185 190

His Arg Glu Asp Gly Ile Leu Thr Lys Leu Ile Cys Lys Val Ser Thr 195 200 205

Leu Arg Ala Leu Cys Gly Arg His Thr Glu Lys Leu Met Ala Phe Lys 210 215 220

Ala Ile Tyr Pro Asp Ile Val Arg Leu His Phe Pro Pro Leu Tyr Lys 235 235 240

Glu Leu Phe Thr

<210> 19

<211> 244

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: fragment of murine  $ROR\alpha$ 

<400> 19

Ser Met Ala Glu Leu Glu His Leu Ala Gln Asn Ile Ser Lys Ser His 1 5 10 15

Leu Glu Thr Cys Gln Tyr Leu Arg Glu Glu Leu Gln Gln Ile Thr Trp
20 25 30

Gln Thr Phe Leu Gln Glu Glu Ile Glu Asn Tyr Gln Asn Lys Gln Arg 35 40 45

Glu Val Met Trp Gln Leu Cys Ala Ile Lys Ile Thr Glu Ala Ile Gln 50 55 60

Tyr Val Val Glu Phe Ala Lys Arg Ile Asp Gly Phe Met Glu Leu Cys 65 70 75 80

Gln Asn Asp Gln Ile Val Leu Leu Lys Ala Gly Ser Leu Glu Val Val 85 90 95

Phe Ile Arg Met Cys Arg Ala Phe Asp Ser Gln Asn Asn Thr Val Tyr 100 105 110

Phe Asp Gly Lys Tyr Ala Ser Pro Asp Val Phe Lys Ser Leu Gly Cys 115 120 125

Glu Asp Phe Ile Ser Phe Val Phe Glu Phe Gly Lys Ser Leu Cys Ser 130 135 140

Met His Leu Thr Glu Asp Glu Ile Ala Leu Phe Ser Ala Phe Val Leu 145 150 155 160

Met Ser Ala Asp Arg Ser Trp Leu Gln Glu Lys Val Lys Ile Glu Lys 165 170 175

Leu Gln Gln Lys Ile Gln Leu Ala Leu Gln His Val Leu Gln Lys Asn 180 185 190

His Arg Glu Asp Gly Ile Leu Thr Lys Leu Ile Cys Lys Val Şer Thr 195 200 205

Leu Arg Ala Leu Cys Gly Arg His Thr Glu Lys Leu Met Ala Phe Lys 210 215 220

Ala Ile Tyr Pro Asp Ile Val Arg Leu His Phe Pro Pro Leu Tyr Lys 225 230 235 240

Glu Leu Phe Thr

<210> 20

<211> 243

<212> PRT

<213> Artificial Sequence

<223> Description of Artificial Sequence: nucleotide sequence coding for a fragment of rat ROR $\beta$ 

<400> 20

Met Ser Glu Ile Asp Arg Ile Ala Gln Asn Ile Ile Lys Ser His Leu

1 5 10 . 15

Glu Thr Cys Gln Tyr Thr Met Glu Glu Leu His Gln Leu Ala Trp Gln
20 25 30

Thr His Thr Tyr Glu Glu Ile Lys Ala Tyr Gln Ser Lys Ser Arg Glu 35 40 45

Ala Leu Trp Gln Gln Cys Ala Ile Gln Ile Thr His Ala Ile Gln Tyr
50 60

Val Val Glu Phe Ala Lys Arg Ile Thr Gly Phe Met Glu Leu Cys Gln 65 70 75 80

Asn Asp Gln Ile Leu Leu Lys Ser Gly Cys Leu Glu Val Val Leu 85 90 95

Glu Gly Lys Tyr Gly Gly Met Gln Met Phe Lys Ala Leu Gly Ser Asp 115 120 125

Asp Leu Val Asn Glu Ala Phe Asp Phe Ala Lys Asn Leu Cys Ser Leu 130 135 140

Gln Leu Thr Glu Glu Glu Ile Ala Leu Phe Ser Ser Ala Val Leu Ile 145 150 155 160

Ser Pro Asp Arg Ala Trp Leu Leu Glu Pro Arg Lys Val Gln Lys Leu 165 170 175

Gln Glu Lys Ile Tyr Phe Ala Leu Gln His Val Ile Gln Lys Asn His 180 185 190

Leu Asp Asp Glu Thr Leu Ala Lys Leu Ile Ala Lys Ile Pro Thr Ile 195 200 205

Thr Ala Val Cys Asn Leu His Gly Glu Lys Leu Gln Val Phe Lys Gln 210 215 220

Ser His Pro Asp Ile Val Asn Thr Leu Phe Pro Pro Leu Tyr Lys Glu 225 230 235 240

Leu Phe Asn

<210> 21

<211> 243

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: fragment of human  $ROR\beta$ 

<400> 21

Met Thr Glu Ile Asp Arg Ile Ala Gln Asn Ile Ile Lys Ser His Leu 1 5 10 15

Glu Thr Cys Gln Tyr Thr Met Glu Glu Leu His Gln Leu Ala Trp Gln
20 25 30

Thr His Thr Tyr Glu Glu Ile Lys Ala Tyr Gln Ser Lys Ser Arg Glu 35 40 45

Ala Leu Trp Gln Gln Cys Ala Ile Gln Ile Thr His Ala Ile Gln Tyr 50 60

Val Val Glu Phe Ala Lys Arg Ile Thr Gly Phe Met Glu Leu Cys Gln 65 70 75 80

Asn Asp Gln Ile Leu Leu Leu Lys Ser Gly Cys Leu Glu Val Val Leu 85 90 95

Val Arg Met Cys Arg Ala Phe Asn Pro Leu Asn Asn Thr Val Leu Phe 100 105 110

Glu Gly Lys Tyr Gly Gly Met Gln Met Phe Lys Ala Leu Gly Ser Asp 115 120 125

Asp Leu Val Asn Glu Ala Phe Asp Phe Ala Lys Asn Leu Cys Ser Leu 130 135 140

Gln Leu Thr Glu Glu Glu Ile Ala Leu Phe Ser Ser Ala Val Leu Ile 145 150 155 160

Ser Pro Asp Arg Ala Trp Leu Ile Glu Pro Arg Lys Val Gln Lys Leu 165 170 175

Gln Glu Lys Ile Tyr Phe Ala Leu Gln His Val Ile Gln Lys Asn His 180 185 190

Leu Asp Asp Glu Thr Leu Ala Lys Leu Ile Ala Lys Ile Pro Thr Ile 195 200 205

Thr Ala Val Cys Asn Leu His Gly Glu Lys Leu Gln Val Phe Lys Gln 210 215 220

Ser His Pro Glu Ile Val Asn Thr Leu Phe Pro Pro Leu Tyr Lys Glu 225 230 235 240

Leu Phe Asn

٠:

<210> 22

<211> 241

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: fragment of human RORy

<400> 22

Leu Thr Glu Ile Glu His Leu Val Gln Ser Val Cys Lys Ser Tyr Arg

1 5 10 15

Glu Thr Cys Gln Leu Arg Leu Glu Asp Leu Leu Arg Gln Arg Ser Asn 20 25 30

Ile Phe Ser Arg Glu Glu Val Thr Gly Tyr Gln Arg Lys Ser Met Trp 35 40 45

Glu Met Trp Glu Arg Cys Ala His His Leu Thr Glu Ala Ile Gln Tyr 50 60

Val Val Glu Phe Ala Lys Arg Leu Ser Gly Phe Met Glu Leu Cys Gln 65 70 75 80

Asn Asp Gln Ile Val Leu Leu Lys Ala Gly Ala Met Glu Val Val Leu 85 90 95

Val Arg Met Cys Arg Ala Tyr Asn Ala Asp Asn Arg Thr Val Phe 100 105 110

Glu Gly Lys Tyr Gly Gly Met Glu Leu Phe Arg Ala Leu Gly Cys Ser 115 120 125

Glu Leu Ile Ser Ser Ile Phe Asp Phe Ser His Ser Leu Ser Ala Leu 130 135 140

His Phe Ser Glu Asp Glu Ile Ala Leu Tyr Thr Ala Leu Val Leu Ile 145 150 155 160

Asn Ala His Arg Pro Gly Leu Gln Glu Lys Arg Lys Val Glu Gln Leu 165 170 175

Gln Tyr Asn Leu Glu Leu Ala Phe His His His Leu Cys Lys Thr His 180 185 190

Arg Gln Ser Ile Leu Ala Lys Leu Pro Pro Lys Gly Lys Leu Arg Ser 195 200 205

Leu Cys Ser Gln His Val Glu Arg Leu Gln Ile Phe Gln His Leu His 210 215 220

Pro Ile Val Val Gln Ala Ala Phe Pro Pro Leu Tyr Lys Glu Leu Phe 225 230 235 240

Ser

<210> 23

<211> 241

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: fragment of murine RORy

<400> 23

Leu Thr Asp Ile Glu Tyr Leu Val Gln Asn Val Cys Lys Ser Phe Arg

1 5 10 15

Glu Thr Cys Gln Leu Arg Leu Glu Asp Leu Leu Arg Gln Arg Thr Asn 20 25 30

Leu Phe Ser Arg Glu Glu Val Thr Ser Tyr Gln Arg Lys Ser Met Trp 35 40 45

Glu Met Trp Glu Arg Cys Ala His His Leu Thr Glu Ala Ile Gln Tyr 50 55 60

Val Val Glu Phe Ala Lys Arg Leu Ser Gly Phe Met Glu Leu Cys Gln 65 70 75 80

Asn Asp Gin Ile Ile Leu Leu Thr Ala Gly Ala Met Glu Val Val Leu 85 90 95

Val Arg Met Cys Arg Ala Tyr Asn Ala Asn Asn His Thr Val Phe 100 105 110

Glu Gly Lys Tyr Gly Gly Val Glu Leu Phe Arg Ala Leu Gly Cys Ser 115 120 125

Glu Leu Ile Ser Ser Ile Phe Asp Phe Ser His Phe Leu Ser Ala Leu 130 135 140

Cys Phe Ser Glu Asp Glu Ile Ala Leu Tyr Thr Ala Leu Val Leu Ile 145 150 155 160

Asn Ala Asn Arg Pro Gly Leu Gln Glu Lys Arg Arg Val Glu His Leu 165 170 175

Gln Tyr Asn Leu Glu Leu Ala Phe His His His Leu Cys Lys Thr His 180 185 190

Arg Gln Gly Leu Leu Ala Lys Leu Pro Pro Lys Gly Lys Leu Arg Ser 195 200 205

Leu Cys Ser Gln His Val Glu Lys Leu Gln Ile Phe Gln His Leu His 210 215 220

Pro Ile Val Val Gln Ala Ala Phe Pro Pro Leu Tyr Lys Glu Leu Phe 225 230 235 240

Ser

47.25)

<210> 24

<211> 243

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: fragment of human  $ROR\alpha$ 

<400> 24

Met Ala Glu Leu Glu His Leu Ala Gln Asn Ile Ser Lys Ser His Leu 1 5 15

Glu Thr Cys Gln Tyr Leu Arg Glu Glu Leu Gln Gln Ile Thr Trp Gln 20 25 30

;

Thr Phe Leu Gln Glu Glu Ile Glu Asn Tyr Gln Asn Lys Gln Arg Glu
35 40 45

Val Met Trp Gln Leu Cys Ala Ile Lys Ile Thr Glu Ala Ile Gln Tyr
50 55 60

Val Val Glu Phe Ala Lys Arg Ile Asp Gly Phe Met Glu Leu Cys Gln 65 70 75 80

Asn Asp Gln Ile Val Leu Leu Lys Ala Gly Ser Leu Glu Val Val Phe
85 90 95

Ile Arg Met Cys Arg Ala Phe Asp Ser Gln Asn Asn Thr Val Tyr Phe 100 105 110

Asp Gly Lys Tyr Ala Ser Pro Asp Val Phe Lys Ser Leu Gly Cys Glu 115 120 125

Asp Phe Ile Ser Phe Val Phe Glu Phe Gly Lys Ser Leu Cys Ser Met 130 135 140

His Leu Thr Glu Asp Glu Ile Ala Leu Phe Ser Ala Phe Val Leu Met 145 150 155 160

Ser Ala Asp Arg Ser Trp Leu Gln Glu Lys Val Lys Ile Glu Lys Leu 165 170 175

Gln Gln Lys Ile Gln Leu Ala Leu Gln His Val Leu Gln Lys Asn His 180 185 190

Arg Glu Asp Gly Ile Leu Thr Lys Leu Ile Cys Lys Val Ser Thr Leu 195 200 205

Arg Ala Leu Cys Gly Arg His Thr Glu Lys Leu Met Ala Phe Lys Ala 210 215 220

Ile Tyr Pro Asp Ile Val Arg Leu His Phe Pro Pro Leu Tyr Lys Glu 225 230 235 240

Leu Phe Thr

<210> 25

<211> 243

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: fragment of murine  $ROR\alpha$ 

<400> 25

Met Ala Glu Leu Glu His Leu Ala Gln Asn Ile Ser Lys Ser His Leu 1 5 10 15

Glu Thr Cys Gln Tyr Leu Arg Glu Glu Leu Gln Gln Ile Thr Trp Gln
20 25 30

Thr Phe Leu Gln Glu Glu Ile Glu Asn Tyr Gln Asn Lys Gln Arg Glu 35 40 45

Val Met Trp Gln Leu Cys Ala Ile Lys Ile Thr Glu Ala Ile Gln Tyr 50 60

Val Val Glu Phe Ala Lys Arg Ile Asp Gly Phe Met Glu Leu Cys Gln 65 70 75 80

Asn Asp Gln Ile Val Leu Leu Lys Ala Gly Ser Leu Glu Val Val Phe 85 90 95

Ile Arg Met Cys Arg Ala Phe Asp Ser Gln Asn Asn Thr Val Tyr Phe 100 105 110

Asp Gly Lys Tyr Ala Ser Pro Asp Val Phe Lys Ser Leu Gly Cys Glu 115 120 125

Asp Phe Ile Ser Phe Val Phe Glu Phe Gly Lys Ser Leu Cys Ser Met 130 135 140

His Leu Thr Glu Asp Glu Ile Ala Leu Phe Ser Ala Phe Val Leu Met 145 150 155 160

Ser Ala Asp Arg Ser Trp Leu Gln Glu Lys Val Lys Ile Glu Lys Leu 165 170 175

Gln Gln Lys Ile Gln Leu Ala Leu Gln His Val Leu Gln Lys Asn His 180 185 190

Arg Glu Asp Gly Ile Leu Thr Lys Leu Ile Cys Lys Val Ser Thr Leu 195 200 205

Arg Ala Leu Cys Gly Arg His Thr Glu Lys Leu Met Ala Phe Lys Ala 210 215 220

Ile Tyr Pro Asp Ile Val Arg Leu His Phe Pro Pro Leu Tyr Lys Glu 225 230 235 240

Leu Phe Thr

<210> 26

<211> 251

<212> PRT <213> Artificial Sequence

<223> Description of Artificial Sequence: nucleotide sequence coding for a fragment of rat RORβ

<400> 26

Gly Gln Leu Ala Pro Gly Ile Thr Met Ser Glu Ile Asp Arg Ile Ala 1 5 15

Gln Asn Ile Ile Lys Ser His Leu Glu Thr Cys Gln Tyr Thr Met Glu 20 25 30

Glu Leu His Gln Leu Ala Trp Gln Thr His Thr Tyr Glu Glu Ile Lys  $35 \hspace{1cm} 40 \hspace{1cm} 45$ 

Ala Tyr Gln Ser Lys Ser Arg Glu Ala Leu Trp Gln Gln Cys Ala Ile 50 55 60

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Gln Ile Thr His Ala Ile Gln Tyr Val Val Glu Phe Ala Lys Arg Ile 65 70 75 80

Thr Gly Phe Met Glu Leu Cys Gln Asn Asp Gln Ile Leu Leu Lys
85 90 95

Ser Gly Cys Leu Glu Val Val Leu Val Arg Met Cys Arg Ala Phe Asn 100 105 110

Pro Leu Asn Asn Thr Val Leu Phe Glu Gly Lys Tyr Gly Gly Met Gln 115 120 125

Met Phe Lys Ala Leu Gly Ser Asp Asp Leu Val Asn Glu Ala Phe Asp 130 135 140

Phe Ala Lys Asn Leu Cys Ser Leu Gln Leu Thr Glu Glu Glu Ile Ala 145 150 155 160

Leu Phe Ser Ser Ala Val Leu Ile Ser Pro Asp Arg Ala Trp Leu Leu 165 170 175

Glu Pro Arg Lys Val Gln Lys Leu Gln Glu Lys Ile Tyr Phe Ala Leu 180 185 190

Gln His Val Ile Gln Lys Asn His Leu Asp Asp Glu Thr Leu Ala Lys 195 200 205

Leu Ile Ala Lys Ile Pro Thr Ile Thr Ala Val Cys Asn Leu His Gly 210 215 220

Glu Lys Leu Gln Val Phe Lys Gln Ser His Pro Asp Ile Val Asn Thr 225 235 240

Leu Phe Pro Pro Leu Tyr Lys Glu Leu Phe Asn 245 250

<210> 27

<211> 251

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: fragment of human  $ROR\beta$ 

<400> 27

Gly Gln Leu Ala Pro Gly Ile Thr Met Thr Glu Ile Asp Arg Ile Ala
1 5 10 15

Gln Asn Ile Ile Lys Ser His Leu Glu Thr Cys Gln Tyr Thr Met Glu
20 25 30

Glu Leu His Gln Leu Ala Trp Gln Thr His Thr Tyr Glu Glu Ile Lys
35 40 45

Ala Tyr Gln Ser Lys Ser Arg Glu Ala Leu Trp Gln Gln Cys Ala Ile 50 55 60

Gln Ile Thr His Ala Ile Gln Tyr Val Val Glu Phe Ala Lys Arg Ile 65 70 75 80

Thr Gly Phe Met Glu Leu Cys Gln Asn Asp Gln Ile Leu Leu Lys 85 90 . 95

Ser Gly Cys Leu Glu Val Val Leu Val Arg Met Cys Arg Ala Phe Asn 100 105 110

Pro Leu Asn Asn Thr Val Leu Phe Glu Gly Lys Tyr Gly Gly Met Gln 115 120 125

Met Phe Lys Ala Leu Gly Ser Asp Asp Leu Val Asn Glu Ala Phe Asp 130 135 140

Phe Ala Lys Asn Leu Cys Ser Leu Gln Leu Thr Glu Glu Glu Ile Ala 145 150 155 160

Leu Phe Ser Ser Ala Val Leu Ile Ser Pro Asp Arg Ala Trp Leu Ile 165 170 175

Glu Pro Arg Lys Val Gln Lys Leu Gln Glu Lys Ile Tyr Phe Ala Leu 180 185 190

Gln His Val Ile Gln Lys Asn His Leu Asp Asp Glu Thr Leu Ala Lys 195 200 205

Leu Ile Ala Lys Ile Pro Thr Ile Thr Ala Val Cys Asn Leu His Gly 210 215 220

Glu Lys Leu Gln Val Phe Lys Gln Ser His Pro Glu Ile Val Asn Thr 225 230 235 240

Leu Phe Pro Pro Leu Tyr Lys Glu Leu Phe Asn 245 250

<210> 28

<211> 249

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: fragment of human RORy

<400> 28

Thr Pro Glu Ala Pro Tyr Ala Ser Leu Thr Glu Ile Glu His Leu Val 1 5 10 15

Gln Ser Val Cys Lys Ser Tyr Arg Glu Thr Cys Gln Leu Arg Leu Glu 20 25 30

Asp Leu Leu Arg Gln Arg Ser Asn Ile Phe Ser Arg Glu Glu Val Thr 35 40 45

Gly Tyr Gln Arg Lys Ser Met Trp Glu Met Trp Glu Arg Cys Ala His
50 55 60

His Leu Thr Glu Ala Ile Gln Tyr Val Val Glu Phe Ala Lys Arg Leu 65 70 75 80

Ser Gly Phe Met Glu Leu Cys Gln Asn Asp Gln Ile Val Leu Lys 85 90 95

- Ala Gly Ala Met Glu Val Val Leu Val Arg Met Cys Arg Ala Tyr Asn 100 105 110
- Ala Asp Asn Arg Thr Val Phe Phe Glu Gly Lys Tyr Gly Gly Met Glu 115 120 125
- Leu Phe Arg Ala Leu Gly Cys Ser Glu Leu Ile Ser Ser Ile Phe Asp 130 135 140
- Phe Ser His Ser Leu Ser Ala Leu His Phe Ser Glu Asp Glu Ile Ala 145 150 155 160
- Leu Tyr Thr Ala Leu Val Leu Ile Asn Ala His Arg Pro Gly Leu Gln 165 170 175
- Glu Lys Arg Lys Val Glu Gln Leu Gln Tyr Asn Leu Glu Leu Ala Phe 180 185 190
- His His Leu Cys Lys Thr His Arg Gln Ser Ile Leu Ala Lys Leu
  195 200 205
- Pro Pro Lys Gly Lys Leu Arg Ser Leu Cys Ser Gln His Val Glu Arg 210 215 220
- Leu Gln Ile Phe Gln His Leu His Pro Ile Val Val Gln Ala Ala Phe 225 230 235 240

Pro Pro Leu Tyr Lys Glu Leu Phe Ser 245

<210> 29

<211> 249

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: fragment of murine RORy

<400> 29

- Ala Pro Glu Val Pro Tyr Ala Ser Leu Thr Asp Ile Glu Tyr Leu Val 1 5 10 15
- Gln Asn Val Cys Lys Ser Phe Arg Glu Thr Cys Gln Leu Arg Leu Glu 20 25 30
- Asp Leu Leu Arg Gln Arg Thr Asn Leu Phe Ser Arg Glu Glu Val Thr
  35 40 45
- Ser Tyr Gln Arg Lys Ser Met Trp Glu Met Trp Glu Arg Cys Ala His
  50 55 60
- His Leu Thr Glu Ala Ile Gln Tyr Val Val Glu Phe Ala Lys Arg Leu 65 70 75 80

Ser Gly Phe Met Glu Leu Cys Gln Asn Asp Gln Ile Ile Leu Leu Thr 85 90 95

Ala Gly Ala Met Glu Val Val Leu Val Arg Met Cys Arg Ala Tyr Asn 100 105 110

Ala Asn Asn His Thr Val Phe Phe Glu Gly Lys Tyr Gly Gly Val Glu 115 120 125

Leu Phe Arg Ala Leu Gly Cys Ser Glu Leu Ile Ser Ser Ile Phe Asp 130 135 140

Phe Ser His Phe Leu Ser Ala Leu Cys Phe Ser Glu Asp Glu Ile Ala 145 150 155 160

Leu Tyr Thr Ala Leu Val Leu Ile Asn Ala Asn Arg Pro Gly Leu Gln 165 170 175

Glu Lys Arg Arg Val Glu His Leu Gln Tyr Asn Leu Glu Leu Ala Phe 180 185 190

His His Leu Cys Lys Thr His Arg Gln Gly Leu Leu Ala Lys Leu 195 200 205

Pro Pro Lys Gly Lys Leu Arg Ser Leu Cys Ser Gln His Val Glu Lys 210 215 220

Leu Gln Ile Phe Gln His Leu His Pro Ile Val Val Gln Ala Ala Phe 225 230 235 240

Pro Pro Leu Tyr Lys Glu Leu Phe Ser 245

<210> 30

<211> 251

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: fragment of human ROR $\alpha$ 

<400> 30

Gly Glu Thr Ser Pro Thr Val Ser Met Ala Glu Leu Glu His Leu Ala 1 5 10 15

Gln Asn Ile Ser Lys Ser His Leu Glu Thr Cys Gln Tyr Leu Arg Glu 20 25 30

Glu Leu Gln Gln Ile Thr Trp Gln Thr Phe Leu Gln Glu Glu Ile Glu 35 40 45

Asn Tyr Gln Asn Lys Gln Arg Glu Val Met Trp Gln Leu Cys Ala Ile 50 55 60

Lys Ile Thr Glu Ala Ile Gln Tyr Val Val Glu Phe Ala Lys Arg Ile 65 70 75 80

Asp Gly Phe Met Glu Leu Cys Gln Asn Asp Gln Ile Val Leu Lys 85 90 95 Ala Gly Ser Leu Glu Val Val Phe Ile Arg Met Cys Arg Ala Phe Asp 100 105 110

- Ser Gln Asn Asn Thr Val Tyr Phe Asp Gly Lys Tyr Ala Ser Pro Asp 115 120 125
- Val Phe Lys Ser Leu Gly Cys Glu Asp Phe Ile Ser Phe Val Phe Glu 130 135 140
- Phe Gly Lys Ser Leu Cys Ser Met His Leu Thr Glu Asp Glu Ile Ala 145 150 155 160
- Leu Phe Ser Ala Phe Val Leu Met Ser Ala Asp Arg Ser Trp Leu Gln
  165 170 175
- Glu Lys Val Lys Ile Glu Lys Leu Gln Gln Lys Ile Gln Leu Ala Leu 180 185 190
- Gln His Val Leu Gln Lys Asn His Arg Glu Asp Gly Ile Leu Thr Lys 195 200 205
- Leu Ile Cys Lys Val Ser Thr Leu Arg Ala Leu Cys Gly Arg His Thr 210 215 220
- Glu Lys Leu Met Ala Phe Lys Ala Ile Tyr Pro Asp Ile Val Arg Leu 225 230 235 240
- His Phe Pro Pro Leu Tyr Lys Glu Leu Phe Thr 245 250
- <210> 31
- <211> 251
- <212> PRT
- <213> Artificial Sequence
- <220>
- <223> Description of Artificial Sequence: fragment of murine  $ROR\alpha$
- <400> 31
- Gly Glu Thr Ser Pro Thr Val Ser Met Ala Glu Leu Glu His Leu Ala
  1 5 10 15
- Gln Asn Ile Ser Lys Ser His Leu Glu Thr Cys Gln Tyr Leu Arg Glu 20 25 30
- Glu Leu Gln Gln Ile Thr Trp Gln Thr Phe Leu Gln Glu Glu Ile Glu 35 40 45
- Asn Tyr Gln Asn Lys Gln Arg Glu Val Met Trp Gln Leu Cys Ala Ile 50 55 60
- Lys Ile Thr Glu Ala Ile Gln Tyr Val Val Glu Phe Ala Lys Arg Ile
  65 70 75 80
- Asp Gly Phe Met Glu Leu Cys Gln Asn Asp Gln Ile Val Leu Leu Lys
  85 90 95

Ala Gly Ser Leu Glu Val Val Phe Ile Arg Met Cys Arg Ala Phe Asp 100 105 110

- Ser Gln Asn Asn Thr Val Tyr Phe Asp Gly Lys Tyr Ala Ser Pro Asp 115 120 125
- Val Phe Lys Ser Leu Gly Cys Glu Asp Phe Ile Ser Phe Val Phe Glu 130 135 140
- Phe Gly Lys Ser Leu Cys Ser Met His Leu Thr Glu Asp Glu Ile Ala 145 150 155 160
- Leu Phe Ser Ala Phe Val Leu Met Ser Ala Asp Arg Ser Trp Leu Gln 165 170 175
- Glu Lys Val Lys Ile Glu Lys Leu Gln Gln Lys Ile Gln Leu Ala Leu 180 185 190
- Gln His Val Leu Gln Lys Asn His Arg Glu Asp Gly Ile Leu Thr Lys 195 200 205
- Leu Ile Cys Lys Val Ser Thr Leu Arg Ala Leu Cys Gly Arg His Thr 210 215 220
- Glu Lys Leu Met Ala Phe Lys Ala Ilë Tyr Pro Asp Ile Val Arg Leu 225 230 235 240
- His Phe Pro Pro Leu Tyr Lys Glu Leu Phe Thr 245 250
- <210> 32
- <211> 252
- <212> PRT
- <213> Artificial Sequence
- <223> Description of Artificial Sequence: nucleotide sequence coding for a fragment of rat ROR $\beta$
- <400> 32
- Gly Gln Leu Ala Pro Gly Ile Thr Met Ser Glu Ile Asp Arg Ile Ala
  1 5 10 15
- Gln Asn Ile Ile Lys Ser His Leu Glu Thr Cys Gln Tyr Thr Met Glu 20 25 30 '
- Glu Leu His Gln Leu Ala Trp Gln Thr His Thr Tyr Glu Glu Ile Lys 35 40 45
- Ala Tyr Gln Ser Lys Ser Arg Glu Ala Leu Trp Gln Gln Cys Ala Ile 50 55 60
- Gln Ile Thr His Ala Ile Gln Tyr Val Val Glu Phe Ala Lys Arg Ile 65 70 75 80
- Thr Gly Phe Met Glu Leu Cys Gln Asn Asp Gln Ile Leu Leu Lys 85 90 95
- Ser Gly Cys Leu Glu Val Val Leu Val Arg Met Cys Arg Ala Phe Asn 100 105 110

Pro Leu Asn Asn Thr Val Leu Phe Glu Gly Lys Tyr Gly Gly Met Gln
115 120 125

Met Phe Lys Ala Leu Gly Ser Asp Asp Leu Val Asn Glu Ala Phe Asp 130 135 140

Phe Ala Lys Asn Leu Cys Ser Leu Gln Leu Thr Glu Glu Glu Ile Ala 145 150 155 160

Leu Phe Ser Ser Ala Val Leu Ile Ser Pro Asp Arg Ala Trp Leu Leu 165 170 175

Glu Pro Arg Lys Val Gln Lys Leu Gln Glu Lys Ile Tyr Phe Ala Leu 180 185 190

Gln His Val Ile Gln Lys Asn His Leu Asp Asp Glu Thr Leu Ala Lys 195 200 205

Leu Ile Ala Lys Ile Pro Thr Ile Thr Ala Val Cys Asn Leu His Gly 210 215 220

Glu Lys Leu Gln Val Phe Lys Gln Ser His Pro Asp Ile Val Asn Thr 225 230 235 240

Leu Phe Pro Pro Leu Tyr Lys Glu Leu Phe Asn Pro 245 250

<210> 33

<211> 252

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: fragment of human  $\mbox{ROR}\beta$ 

<400> 33

Gly Gln Leu Ala Pro Gly Ile Thr Met Thr Glu Ile Asp Arg Ile Ala 1 5 10 15

Gln Asn Ile Ile Lys Ser His Leu Glu Thr Cys Gln Tyr Thr Met Glu 20 25 30 .

Glu Leu His Gln Leu Ala Trp Gln Thr His Thr Tyr Glu Glu Ile Lys
35 40 45

Ala Tyr Gln Ser Lys Ser Arg Glu Ala Leu Trp Gln Gln Cys Ala Ile 50 55 60

Gln Ile Thr His Ala Ile Gln Tyr Val Val Glu Phe Ala Lys Arg Ile 65 70 75 80

Thr Gly Phe Met Glu Leu Cys Gln Asn Asp Gln Ile Leu Leu Leu Lys 85 90 95

Ser Gly Cys Leu Glu Val Val Leu Val Arg Met Cys Arg Ala Phe Asn 100 105 110

Pro Leu Asn Asn Thr Val Leu Phe Glu Gly Lys Tyr Gly Gly Met Gln 115 120 125

Met Phe Lys Ala Leu Gly Ser Asp Asp Leu Val Asn Glu Ala Phe Asp 130 135 140

Phe Ala Lys Asn Leu Cys Ser Leu Gln Leu Thr Glu Glu Glu Ile Ala 145 150 155 160

Leu Phe Ser Ser Ala Val Leu Ile Ser Pro Asp Arg Ala Trp Leu Ile 165 170 175

Glu Pro Arg Lys Val Gln Lys Leu Gln Glu Lys Ile Tyr Phe Ala Leu 180 185 190

Gln His Val Ile Gln Lys Asn His Leu Asp Asp Glu Thr Leu Ala Lys 195 200 205

Leu Ile Ala Lys Ile Pro Thr Ile Thr Ala Val Cys Asn Leu His Gly 210 215 220

Glu Lys Leu Gln Val Phe Lys Gln Ser His Pro Glu Ile Val Asn Thr 225 230 235 240

Leu Phe Pro Pro Leu Tyr Lys Glu Leu Phe Asn Pro
245 250

<210> 34

<211> 250

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: fragment of human RORy

<400> 34

Thr Pro Glu Ala Pro Tyr Ala Ser Leu Thr Glu Ile Glu His Leu Val 1 5 10 15

Gln Ser Val Cys Lys Ser Tyr Arg Glu Thr Cys Gln Leu Arg Leu Glu 20 .25 30

Asp Leu Leu Arg Gln Arg Ser Asn Ile Phe Ser Arg Glu Glu Val Thr 35 40 45

Gly Tyr Gln Arg Lys Ser Met Trp Glu Met Trp Glu Arg Cys Ala His
50 55 60

His Leu Thr Glu Ala Ile Gln Tyr Val Val Glu Phe Ala Lys Arg Leu 65 70 75 80

Ser Gly Phe Met Glu Leu Cys Gln Asn Asp Gln Ile Val Leu Lys 85 90 95

Ala Gly Ala Met Glu Val Val Leu Val Arg Met Cys Arg Ala Tyr Asn 100 105 110

Ala Asp Asn Arg Thr Val Phe Phe Glu Gly Lys Tyr Gly Gly Met Glu
115 120 125

Leu Phe Arg Ala Leu Gly Cys Ser Glu Leu Ile Ser Ser Ile Phe Asp 130 135 140

Phe Ser His Ser Leu Ser Ala Leu His Phe Ser Glu Asp Glu Ile Ala 145 150 155 160

Leu Tyr Thr Ala Leu Val Leu Ile Asn Ala His Arg Pro Gly Leu Gln 165 170 175

Glu Lys Arg Lys Val Glu Gln Leu Gln Tyr Asn Leu Glu Leu Ala Phe 180 185 190

His His Leu Cys Lys Thr His Arg Gln Ser Ile Leu Ala Lys Leu 195 200 205

Pro Pro Lys Gly Lys Leu Arg Ser Leu Cys Ser Gln His Val Glu Arg 210 215 220

Leu Gln Ile Phe Gln His Leu His Pro Ile Val Val Gln Ala Ala Phe 225 230 235 240

Pro Pro Leu Tyr Lys Glu Leu Phe Ser Thr 245

<210> 35

<211> 250

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: fragment of murine ROR $\gamma$ 

<400> 35

Ala Pro Glu Val Pro Tyr Ala Ser Leu Thr Asp Ile Glu Tyr Leu Val 1 5 10 15

Gln Asn Val Cys Lys Ser Phe Arg Glu Thr Cys Gln Leu Arg Leu Glu 20 25 30

Asp Leu Leu Arg Gln Arg Thr Asn Leu Phe Ser Arg Glu Glu Val Thr 35 40 45

Ser Tyr Gln Arg Lys Ser Met Trp Glu Met Trp Glu Arg Cys Ala His 50 55 60

His Leu Thr Glu Ala Ile Gln Tyr Val Val Glu Phe Ala Lys Arg Leu 65 70 75 80

Ser Gly Phe Met Glu Leu Cys Gln Asn Asp Gln Ile Ile Leu Leu Thr
85 90 95

Ala Gly Ala Met Glu Val Val Leu Val Arg Met Cys Arg Ala Tyr Asn

Ala Asn Asn His Thr Val Phe Phe Glu Gly Lys Tyr Gly Gly Val Glu

Leu Phe Arg Ala Leu Gly Cys Ser Glu Leu Ile Ser Ser Ile Phe Asp 130 135 140

Phe Ser His Phe Leu Ser Ala Leu Cys Phe Ser Glu Asp Glu Ile Ala 145 150 155 160

Leu Tyr Thr Ala Leu Val Leu Ile Asn Ala Asn Arg Pro Gly Leu Gln 165 170 175

Glu Lys Arg Arg Val Glu His Leu Gln Tyr Asn Leu Glu Leu Ala Phe 180 185 190

His His Leu Cys Lys Thr His Arg Gln Gly Leu Leu Ala Lys Leu 195 200 205

Pro Pro Lys Gly Lys Leu Arg Ser Leu Cys Ser Gln His Val Glu Lys 210 220

Leu Gln Ile Phe Gln His Leu His Pro Ile Val Val Gln Ala Ala Phe 225 230 235 240

Pro Pro Leu Tyr Lys Glu Leu Phe Ser Thr 245

<210> 36

<211> 252

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: fragment of human  $ROR\alpha$ 

<400> 36

Gly Glu Thr Ser Pro Thr Val Ser Met Ala Glu Leu Glu His Leu Ala  $1 \hspace{1cm} 5 \hspace{1cm} 10 \hspace{1cm} 15$ 

Gln Asn Ile Ser Lys Ser His Leu Glu Thr Cys Gln Tyr Leu Arg Glu 20 25 30

Glu Leu Gln Gln Ile Thr Trp Gln Thr Phe Leu Gln Glu Glu Ile Glu 35 40 45

Asn Tyr Gln Asn Lys Gln Arg Glu Val Met Trp Gln Leu Cys Ala Ile 50 55 60

Lys Ile Thr Glu Ala Ile Gln Tyr Val Val Glu Phe Ala Lys Arg Ile 65 70 75 80

Asp Gly Phe Met Glu Leu Cys Gln Asn Asp Gln Ile Val Leu Lys 85 90 95

Ala Gly Ser Leu Glu Val Val Phe Ile Arg Met Cys Arg Ala Phe Asp 100 105 110

Ser Gln Asn Asn Thr Val Tyr Phe Asp Gly Lys Tyr Ala Ser Pro Asp 115 120 125

Val Phe Lys Ser Leu Gly Cys Glu Asp Phe Ile Ser Phe Val Phe Glu 130 135 140

Phe Gly Lys Ser Leu Cys Ser Met His Leu Thr Glu Asp Glu Ile Ala 145 150 155 160

Leu Phe Ser Ala Phe Val Leu Met Ser Ala Asp Arg Ser Trp Leu Gln 165 170 175

Glu Lys Val Lys Ile Glu Lys Leu Gln Gln Lys Ile Gln Leu Ala Leu 180 185 190

Gln His Val Leu Gln Lys Asn His Arg Glu Asp Gly Ile Leu Thr Lys 195 200 205

Leu Ile Cys Lys Val Ser Thr Leu Arg Ala Leu Cys Gly Arg His Thr 210 215 220

Glu Lys Leu Met Ala Phe Lys Ala Ile Tyr Pro Asp Ile Val Arg Leu 225 230 235 240

His Phe Pro Pro Leu Tyr Lys Glu Leu Phe Thr Ser 245 250

<210> 37

<211> 252

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: fragment of murine  $ROR\alpha$ 

<400> 37

Gly Glu Thr Ser Pro Thr Val Ser Met Ala Glu Leu Glu His Leu Ala 1 5 10 15

Gln Asn Ile Ser Lys Ser His Leu Glu Thr Cys Gln Tyr Leu Arg Glu
20 25 30

Glu Leu Gln Gln Ile Thr Trp Gln Thr Phe Leu Gln Glu Glu Ile Glu 35 40 45

Asn Tyr Gln Asn Lys Gln Arg Glu Val Met Trp Gln Leu Cys Ala Ile
50 55 60

Lys Ile Thr Glu Ala Ile Gln Tyr Val Val Glu Phe Ala Lys Arg Ile 65 70 75 80

Asp Gly Phe Met Glu Leu Cys Gln Asn Asp Gln Ile Val Leu Leu Lys 85 90 95

Ala Gly Ser Leu Glu Val Val Phe Ile Arg Met Cys Arg Ala Phe Asp

Ser Gln Asn Asn Thr Val Tyr Phe Asp Gly Lys Tyr Ala Ser Pro Asp 115 120 ' 125

Val Phe Lys Ser Leu Gly Cys Glu Asp Phe Ile Ser Phe Val Phe Glu 130 135 140

Phe Gly Lys Ser Leu Cys Ser Met His Leu Thr Glu Asp Glu Ile Ala 145 150 155 160

Leu Phe Ser Ala Phe Val Leu Met Ser Ala Asp Arg Ser Trp Leu Gln 165 170 175

- Glu Lys Val Lys Ile Glu Lys Leu Gln Gln Lys Ile Gln Leu Ala Leu 180 185 190
- Gln His Val Leu Gln Lys Asn His Arg Glu Asp Gly Ile Leu Thr Lys 195 200 205
- Leu Ile Cys Lys Val Ser Thr Leu Arg Ala Leu Cys Gly Arg His Thr 210 215 220
- Glu Lys Leu Met Ala Phe Lys Ala Ile Tyr Pro Asp Ile Val Arg Leu 225 230 235 240
- His Phe Pro Pro Leu Tyr Lys Glu Leu Phe Thr Ser 245 250

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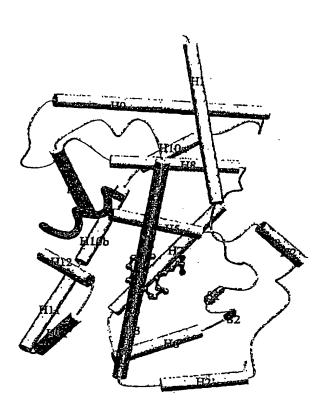
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[Continued on next page]

(54) Title: FRAGMENTS OF THE RETINOIC ACID-RELATED ORPHAN RECEPTOR (ROR) COMPRISING THE LIG AND BINDING DOMAIN (LBD), CRYSTAL STRUCTURE OF THE LBD OF ROR-BETA AND THEIR APPLICATIONS



(57) Abstract: The invention relates to polypeptides derived from the retinoic acid-related orphan receptor (ROR) in mammals, characterized in that they are delimited in their N-terminal extremity by an amino-acid located between positions 1 to 209, and in their C-terminal extremity by an amino-acid located between positions 450 to 452 of the rat RORB, α, or γ, or by an amino-acid located at corresponding positions in nuclear receptor ROR of other subtypes than  $\alpha$ ,  $\beta$  and  $\gamma$ , and/or of the other mammals. The invention also relates to the use of these polypeptides, or of the molecular complexes or the crystals containing them, for carrying out: -a process for the screening of a ROR-LBD ligand which is an agonist, or an antagonist of said receptor, - or a process for the analysis of the tridimensional structure of the complexes formed with said polypeptides, molecular complexes or crystals and a particular compound.

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For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

International Application No
PCT/EP 02/05024

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According to	International Patent Classification (IPC) or to both national classification	ation and IPC	
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Documental	ion searched other than minimum documentation to the extent that s	uch documents are included in the fields searched	
Electronic da	ata base consulted during the international search (name of data bas	se and, where practical, search terms used)	
BIOSIS	, EPO-Internal, MEDLINE, WPI Data, E	MBL .	
C. DOCUME	ENTS CONSIDERED TO BE RELEVANT		
Category °	Citation of document, with indication, where appropriate, of the rele	evant passages Relevant to claim No.	
X	GREINER ERICH F ET AL: "Function analysis of retinoid Z receptor b brain-specific nuclear orphan receptor proceedings of the NATIONAL ACADE SCIENCES OF THE UNITED STATES, vol. 93, no. 19, 1996, pages 1010 XP002194193 1996 ISSN: 0027-8424 the whole document page 10106, column 1, paragraph 3 1,2	eta, a eptor." MY OF 5-10110,	
Ϋ́χ Furti	her documents are listed in the continuation of box C.	X Patent family members are listed in annex.	
"A" docume consider in the considering	*T' later document published after the International filing date or priority date and not in conflict with the application but considered to be of particular relevance considered to be of particular relevance in understand the principle or theory underlying the invention cannot be considered novel or cannot be considered to establish the publication date of another citation or other special reason (as specified)  'O' document referring to an oral disclosure, use, exhibition or other means  'P' document upblished prior to the international filing date but later than the priority date claimed  'Special categories of cited document published after the international filing date or priority date and not in conflict with the application but cited to understand the priority date and not in conflict with the application but cited to understand the priority date claimed invention cannot be considered novel or cannot be considered novel or cannot be considered to involve an inventive step when the document is combined with one or more other such document is co		
Date of the	actual completion of the international search	Date of mailing of the international search report	
2	9 November 2002	16/12/2002	
Name and r	mailing address of the ISA  European Patent Office, P.B. 5818 Patentlaan 2  NL – 2280 HV Rijswijk  Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  Fax (+31-70) 340-3016	Authorized officer Petri, B	

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Int ional Application No PCT/EP 02/05024

Category °	DISTRICT CONSIDERED TO BE RELEVANT  Citation of document, with indication, where appropriate, of the relevant passages	Delevent to a bin Ma
<del></del>	, , , , and the second of the	Relevant to claim No.
X	GREINER ERICH F ET AL: "Differential ligand-dependent protein-protein interactions between nuclear receptors and a neuronal-specific cofactor."  PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES, vol. 97, no. 13, 30 June 2000 (2000-06-30), pages 7160-7165, XP002194194  June 30, 2000  ISSN: 0027-8424  the whole document figure 2	6,7,9-13
X	DATABASE EMBL 'Online! retrieved from EBI Database accession no. P35398; P51448; Q92753; P45446; P51449; P51450 XP002221987	6,7,9-13
Y	h/mROR-alpha; h/rROR-beta; h/mROR-gamma 1.6.1994; 1.10.1996; 1.11.1997; 1.11.1995; 1.10.1996; 1.10.1996; annotated LBD the whole document	14-17,21
(	WO 99 50660 A (RASPE ERIC ;BONHOMME YVES (FR); MERCK PATENT GMBH (US)) 7 October 1999 (1999-10-07) claims 1-17 the whole document	6,7, 9-13, 18-20
	WO 00 24757 A (TULARIK INC) 4 May 2000 (2000-05-04)  claims 25-43; figures 1,2 the whole document	6,7, 9-13, 18-20
	WO 01 26737 A (NOVARTIS ERFIND VERWALT GMBH; KNEISSEL MICHAELA (CH); NOVARTIS AG) 19 April 2001 (2001-04-19) claims 3-5 the whole document	6,7, 9-13, 18-20
	GILLILAND G L ET AL: "Crystallization of biological macromolecules for X-ray diffraction studies" CURRENT OPINION IN STRUCTURAL BIOLOGY, CURRENT BIOLOGY LTD., LONDON, GB, vol. 6, no. 5, October 1996 (1996-10), pages 595-603, XP002128062 ISSN: 0959-440X the whole document	14-17,21
	- <u></u> -/	

Intc.....nal Application No PCT/EP 02/05024

C.(Continu	ation) DOCUMENTS CONSIDERED TO BE RELEVANT	FC1/EF 02/05024
Category •	Cilation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Υ	ABOLA ENRIQUE ET AL: "Automation of X-ray crystallography." NATURE STRUCTURAL BIOLOGY, vol. 7, no. Supplement, November 2000 (2000-11), pages 973-977, XP001062873 ISSN: 1072-8368 the whole document	14-17,21
Y	BOURGUET WILLIAM ET AL: "Crystal structure of a heterodimeric complex of RAR and RXR ligand-binding domains." MOLECULAR CELL, vol. 5, no. 2, February 2000 (2000-02), pages 289-298, XP002194192 ISSN: 1097-2765 page 296, column 2, paragraph 3 the whole document	14-17,21
A	NOLTE R T ET AL: "LIGAND BINDING AND CO-ACTIVATOR ASSEMBLY OF THE PEROXISOME PROLIFERATOR-ACTIVATED RECEPTOR-GAMMA" NATURE, MACMILLAN JOURNALS LTD. LONDON, GB, vol. 395, 10 September 1998 (1998-09-10), pages 137-143, XP002906503 ISSN: 0028-0836 Discloses PDB:2PRG; identical topology (RMSD: 1.8A) with PDB:1K4W figure 1; table 2	8,20,21
P,X	STEHLIN CATHERINE ET AL: "X-ray structure of the orphan nuclear receptor RORbeta ligand-binding domain in the active conformation."  EMBO (EUROPEAN MOLECULAR BIOLOGY ORGANIZATION) JOURNAL, vol. 20, no. 21, 1 November 2001 (2001-11-01), pages 5822-5831, XP002221986 ISSN: 0261-4189 the whole document	6-21

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Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)
(Continuation of item 1 of first sheet)
This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:
Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:
2. X Claims Nos.: 1-5 because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:  See FURTHER INFORMATION sheet PCT/ISA/210
3. Claims Nos.: because they are dependent daims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).
Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)
This International Searching Authority found multiple inventions in this international application, as follows:
1. As all required additional search fees were timely paid by the applicant, this international Search Report covers all searchable claims.
2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
Remark on Protest  The additional search fees were accompanied by the applicant's protest.  No protest accompanied the payment of additional search fees.

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### FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 1-5

Present claims 1-5 relate to a population of vaguely defined possible polypeptides.

The claims contain so many options that a lack of clarity and/or conciseness within the meaning of Article 6 PCT arises to such an extent as to render a meaningful search of the claims impossible.

The term "derived = deriveable" leaves the structural properties of the claimed polypeptides open to speculation. In its extreme interpretation any structural limitation is abolished.

The definition of N- and/or C-terminally truncated ROR-variants by reference to positions as represented on Fig. 3 is unclear and confusing: First of all, Fig. 3 does not contain all positions as claimed (e.g. positions 1-199 are missing). Furthermore, Fig. 3 depicts only partial h/mROR alpha-gamma molecules, leaving it open to speculation as to which residues of non-aligned molecules would correspond to the claimed boundaries.

Orphan receptors are receptors for which no ligands are known. Hence the functional definition of claim 3 does not impose any further limitation and is to be considered as a mere desireable property.

Reference to positions 459, 454, 458 in claim 4 is a contradiction in terms to claim 1, further obscuring the subject-matter for which protection is sought. Furthermore not all the claimed molecules have the claimed non-conserved cysteine residues.

In summary claims 1-5 contain so many obscurities, open terms and contradiction in terms, which render it difficult, if not impossible, to determine the matter for which protection is sought. As a consequence, the present application fails to comply with the clarity and conciseness requirements of Article 6 PCT (see also Rule 6.1(a) PCT) to such an extent that a meaningful search for claims 1-5 is impossible. Consequently, the search has been carried out for those parts of the application which do appear to be clear and concise, namely the subject-matter relating to Seq.Id.Nos. 2-37, of claim 6.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

Information on patent family members

Int anal Application No PCT/EP 02/05024

Patent document Publication Patent form				101/21 02/03024	
	Publication date		Patent family member(s)	Publication date	
Α	07-10-1999	FR AU AU CA WO EP NZ	2776388 A1 752062 B2 3521599 A 2326141 A1 9950660 A1 1070253 A1 507761 A	24-09-1999 05-09-2002 18-10-1999 07-10-1999 07-10-1999 24-01-2001 25-10-2002	
A 	04-05-2000	UA WO	1210300 A 0024757 A1	15-05-2000 04-05-2000	
Α .	19-04-2001	AU WO EP	1134601 A 0126737 A2 1239922 A2	23-04-2001 19-04-2001 18-09-2002	
	A	A 04-05-2000	A 04-05-2000 AU WO	Publication date Patent family member(s)  A 07-10-1999 FR 2776388 A1 AU 752062 B2 AU 3521599 A CA 2326141 A1 W0 9950660 A1 EP 1070253 A1 NZ 507761 A  A 04-05-2000 AU 1210300 A W0 0024757 A1  A 19-04-2001 AU 1134601 A W0 0126737 A2	